

GROWTH & DEVELOPMENT

Growth

- It is increase in the size of the body as a whole or of its individual parts, due to multiplication of cells & intracellular substance.

Development

- It is functional maturation of organs and systems with acquisition of skills and adaptation to society.
- Both growth & development go parallel to each other during normal life. However sometimes there is delay or stoppage in one of them in some pathological conditions.

Periods of human life

1. Intrauterine life

- Embryonic life ---- 1st trimester
- Fetal life ---- 2nd & 3rd trimester

2. Peri-natal:

- It extends from the start of labor till the end of the 1st 24 hr of life.

3. Neonatal period:

- The first 4 wks of life (28 days).

4. Infancy:

- Early infancy: 1st year.
- Late infancy: 2nd year

5. Childhood period.

- Preschool age: 2-6 years.
- School age: 6-10 years in females.
6-12 years in males..

6. Adolescence:

- Females: 10 -15 years.
- Males: 12-17 years.

7. Adulthood

- Females >15
- Males >17.

N.B.: There is overlap between peri natal & neonatal.

Factors Affecting Growth & development

1- Genetic factors.

2-Environmental factors:

- Racial.
- Geographical.
- Nutritional.

3-Psychological & emotional factors. → Mother ---infant relationship.

4-Endocrinal factors

5- Activities.

6-Chronic illness.

7- Secular trend

8-Socioeconomic factors.

VISIT...

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Assessment of growth

Growth assessment by anthropometric measurements can be done through

A. Non-specific (basic) measurements:

Weight, height or length, body proportions, growth velocity, mid-arm circumference, skin fold thickness & skull circumference.

Normal body proportions are:

- o Span to total height ratio around 1.0 at all ages.
- o Upper to lower segment ratio is around 1.7 in the neonatal period, decreasing to 1.4 at age 4-5 years & to 1.0 by age 10-12 years

B. Specific measurements:

Chest circumference & thoracic index, these can be done for special children for special purposes as for research work

Weight

- The weight of the newborn infant averages about 3.25 Kg.
- There is physiological weight loss which is about 5-10 % of body weight. It is regained back by 10 days of age.
- In the 1st 4 months there is weight increase by $\frac{3}{4}$ kg/ month.
- In the 2nd 4 months there is weight increase by $\frac{1}{2}$ kg / month.
- In the 3rd 4 months there is weight increase by $\frac{1}{4}$ kg/month.
- So the baby double his weight by the 4th month & triples his weight by the end of the 1st year.

Weight	Kg
At birth	3-3.5
3-12 months	$\frac{\text{Age (m)} + 9}{2}$
1-6 years	$\text{Age (years)} \times 2 + 8$
7-12 years	$\frac{\text{Age (years)} \times 7 - 5}{2}$

Height or Length

- Length: measured in infancy period (up to 2 years) or in children who are unable to stand without assistant.
- Height: measured in children who are able to stand without assistant.

Height	Centimeters
At birth	50
At 1 year	75
2-12 years	$\text{Age (years)} \times 5 + 80$ Or $\text{Age (years)} \times 6 + 77$

Ossification development

Bone age can be determined by the appearance of ossific centers in X-ray films as follows:
At birth there are 6 centers of ossification:

1. Distal end of the femur.
2. Proximal end of the tibia.
3. Talus.
4. Calcaneous.
5. Cuboids.
6. Head of the humerus.

The carpal bones:

They are 8 in number:

1st one appears in the 1st 6 months.

2nd one appears at the end of the 1st year.

Then, one carpal bone each year up to 6 years.

The 8th carpal bone appears at 12 years.

Causes of delayed bone age:

1. Hypothyroidism.
2. Hypopituitarism.
3. Hypoparathyroidism.
4. Severe under & mal-nutrition.

Causes of advanced bone age:

1. Thyrotoxicosis.
2. Excess GH.
3. Hyperparathyroidism.
4. Precocious puberty.
5. Congenital adrenal hyperplasia.
6. Iatrogenic with androgen therapy.

Skin fold thickness

This measures the subcutaneous fat because we measure the skin & S.C. tissue, this is measured over:

1. The biceps.
2. The triceps
3. Subscapular area.
4. Supra-iliac areas.

It can be measured by "Harpender's skin fold caliber".

Skull circumference, fontanels

Look.....Clinical note.

Teething:

1. Temporary (1st milk, deciduous) teeth

They are 20 in number, 10 in each jaw.

- At 6 months lower central incisors.

8 months upper central incisors.

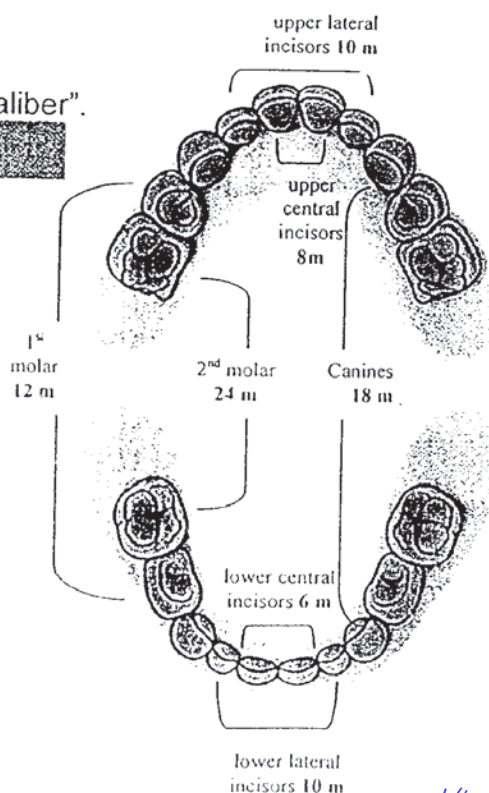
10 months upper lateral incisors.

10-12 months lower lateral incisors.

12-15 months 1st molars.

18 months canines.

24 months 2nd molars.



2. Permanent teeth:

They are 32 in number.

- At 6 Years 1st molar.
- 8 years central incisors.
- 9 years lateral incisors.
- 10 years canines.
- 11 years 1st premolars.
- 12 years 2nd premolars.
- 13 years 2nd molars.
- 17-25 years 3rd molars.

Causes of delayed teething:

1. Rickets.
2. Cretinism.
3. Down S.
4. Under-nutrition & malnutrition.

Premature eruption of teeth: in congenital syphilis.

Analysis and interpretation of growth chart:

- The standard growth chart is based on data collected from a big number of infants and children from birth to 18 years in a given community.
- It is composed of several percentile curves most important are weight, height or length and head circumference for age.
- The X-axis on the curve represents the age and the measured variable on the axis. The percentile curve indicates the percentage of children at a given age whose measured value falls below the corresponding value indicated on the axis.
- By definition the 50th percentile is the median i.e. the value above (and below), which 50% of the observed values fall.
- The normal range of the observed variable lies between the 5th and 95th percentile lines. Values between 3rd and 5th percentiles and those between 95th and 97th percentile lines are considered suspicious of abnormality and should be followed up more frequently. Values below 3rd and above 97th percentile are definitely abnormal.
- Disparities in growth between developed and developing countries reflect nutritional rather than genetic differences.
- Curves may be less applicable to adolescents as growth during adolescence is temporally linked to the onset of puberty, which varies widely.
- Specialized charts have also been developed for children with various conditions, including Down, Turner, Klinefelter syndromes and achondroplasia.

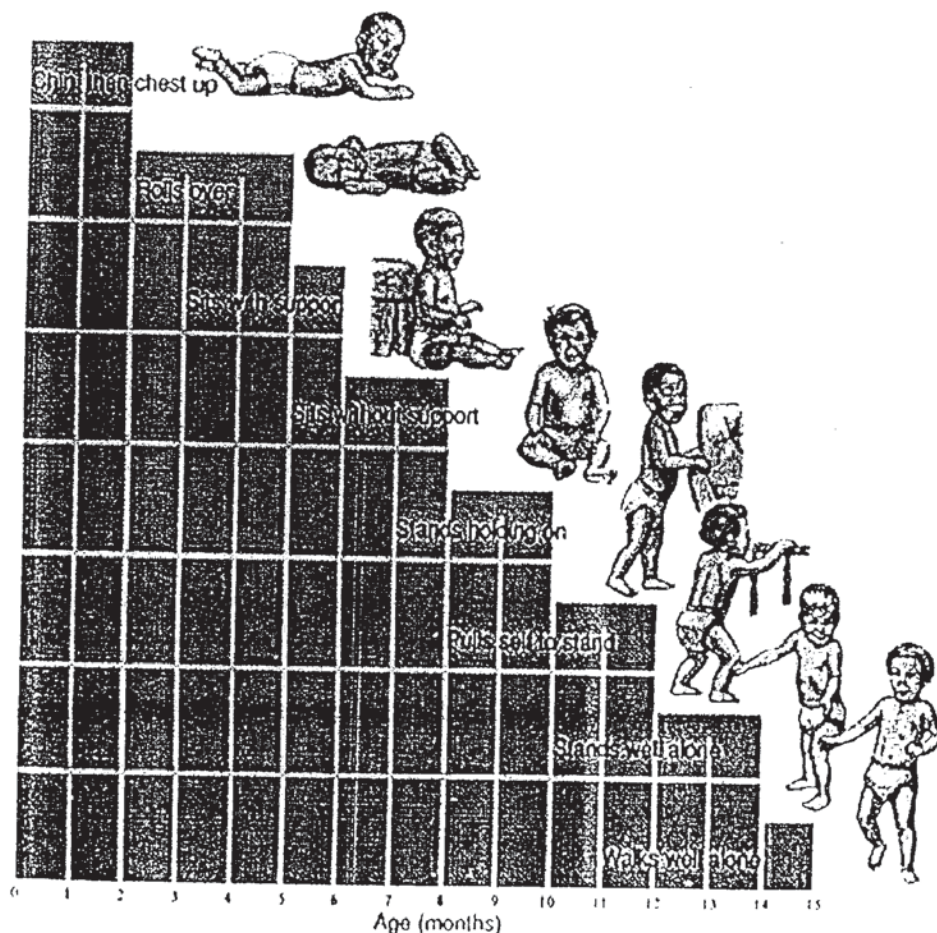
Assessment of Development

Characteristic features of development:

- 1- It is a continuous process.
- 2- It always follows the same pattern.
- 3- It is always cephalo-caudal progress.

Gross motor development

2 month	Chin then chest up
3 months	Neck support
6 month	Rolls over
4-6 month	sitting supported
6-8 month	sitting unsupported
8-10 month	Stands hold on
9-12 month	Pull himself to stand & crawls free
12-14 month	Stand well alone & walk supported with one hand.
11-15 month	Walk well alone
18 months	Ascending upstairs in a child manner.
24 months	Descending in a child manner.
3 years	Ascending upstairs in an adult manner
4 years	Descending in an adult manner
5 years	Can hold on one limb.



Fine motor (Manipulative)

- At 4 m $\Rightarrow$ Brings hands together to play with them
 6m $\Rightarrow$ Grasp bottle, bring toes to mouth.
 7m $\Rightarrow$ can transfer a toy from one hand to another.
 9m $\Rightarrow$ can hold objects between thumb & forefingers.
 10 m $\Rightarrow$ Point at object with index finger.



6 month

7 month

9 month

Speech

- | | |
|------------|---|
| At 6 weeks | Throaty sounds |
| 6ms | 1 syllable of word e.g. pa, ma, da |
| 9 mo | 2 syllables of word e.g. papa, mama, dada |
| 1 yr | one & two words: |
| 1.5 yr | 3 - 10 words (not necessarily meaningful). , show parts of the body |
| 2 yr | 2 words in a sentence |
| 3 yr | says his name, age, sex. |
| 4-5 yr | can tell a story. |



1 year



1.5 year



2 year

Pediatrics

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growth & development

Social & personal development:

At 2m	smiles in response to stimuli
4m	laughs on social contact & prefer social contact.
4-5m	recognizes his mother
10 ms	respond to his name – wave bye bye
12 ms	simple ball games.

Feeding:

The child feeds himself from the age of 2.5 yr.



Dressing:

Can dress himself at the age of 3 yr.

Sphincteric control:

- ❖ Automatic bladder (local spinal reflex) during the 1st year.
- ❖ The mother trains her baby to sit on the potty at 5-6 months $\Rightarrow$ conditioned reflex on touching the potty.
- ❖ Early voluntary control (incomplete) starts at 15 - 18 mo $\Rightarrow$ the baby aware of being wet, Asks to go but usually late (no voluntary inhibition).
- ❖ At the age of 2 years $\Rightarrow$ calls before & controls by day.
- ❖ At the age of 3 years $\Rightarrow$ dry by day & night.
- ❖ A child's average bladder capacity = (age in years +1) X 30 = average voided volume
- ❖ Urine is produced from the kidney is about 60 ml/hr

Special senses:

Taste: present since birth.

Vision:

- ❖ He can see at birth with diminished visual acuity.
- ❖ Can fixate on moving objects at 1 month.
- ❖ Can follow moving objects 180 degrees.
- ❖ Proper coordination of eye movements at 4-6 ms.

Hearing:

- ❖ At birth: can hear without following the source of sound.
- ❖ At 6 months: following the source of the sound.



Puberty

Definition

Transition period between childhood & adulthood periods during which reproductive function is attained.

Changes occurs during this periods

- ❖ The secondary sexual characteristics appear.
- ❖ Adolescent growth spurt occurs.
- ❖ The gonads start to produce mature gametes.
- ❖ Major physiological changes occur.

Physical Changes of puberty

Pubic hair development

Tanner I	Non
Tanner II	Few darker hair along labia or at the base of the penis
Tanner III	Curly pigmented hairs across pubes
Tanner IV	Small adult configuration
Tanner V	Adult configuration with spread to inner thigh & may spread to linea alba in some males

Male genital development

Tanner I	Prepubertal
Tanner II	Testes enlarge (4ml); scrotum larger, reddened and skin coarser
Tanner III	Penis enlarges, initially in length, continued growth of testes and scrotum
Tanner IV	Penis growth in length & breadth; continued growth of testes & scrotum that becomes pigmented
Tanner V	All are in adult size

Female breast development

Tanner I	Prepubertal
Tanner II	Areola enlargement with breast bud
Tanner III	Enlargement of breast and areola as single mound
Tanner IV	Projection of areola above breast as double mound
Tanner V	Adult; papilla projects out of areola that is part of breast contour

Precocious puberty:

If these changes are noted prior to 8 years in girls & 9 years in boys.

Delayed puberty:

If these changes do not occur up to 13 years in girls & 14 years in boys.

Hormonal Changes of puberty

- ❖ Adrenarche: increase DHEA-S production by zona reticularis of adrenal gland, precedes the onset of puberty.
- ❖ Gn-RH secretion by the hypothalamus is responsible for initiation of puberty under the effect of plethora of central & peripheral signals: excitatory amino acids, other neurotransmitters such as GABA, gonadal sex steroids, adrenal & thyroid hormones.....etc

Enuresis

Definition

Inability to control urination till the age of 5 years

Classifications

- I. **Primary or secondary:**
 - ❖ Primary: the child has never controlled before.
 - ❖ Secondary: The child has achieved voluntary control for at least 6 months
- II. **Nocturnal or Diurnal:**
 - ❖ Nocturnal: failure of control only during sleep.
 - ❖ Diurnal: failure of control only during day & night.
- III. **Monosymptomatic or Polysymptomatic:**
 - ❖ Monosymptomatic (MNE): bed wetting without other voiding disorders.
 - ❖ Polysymptomatic (PNE): associated with bladder symptoms as urgency.

Monosymptomatic Nocturnal Enuresis

Etiology

1. **Psychological factors**: stressful circumstances as;
 - ❖ Aggressive parents.
 - ❖ Coming of new sibling.
 - ❖ Loss of one of the family.
2. **Loss circadian rhythm of ADH**: $\Rightarrow$ nocturnal Polyuria.
3. **Excessive fluid intake at night.**
4. **Maturation & developmental delay**: delayed recognition & response to full bladder.
5. **Genetic factors**: if there is associated family history.
6. **Functional bladder capacity**: $\downarrow\downarrow$ functional capacity of the bladder.
7. **Sleep arousal dysfunction**: deep sleep or arousal disturbances & delay in perception of bladder fullness.

D. D.

1. Entrobiasis:
2. Diabetes mellitus or insipidus.
3. Urinary tract diseases.
4. Spina bifida with fibrous tissue stretching the spinal cord.
5. Anomalies in the sphincter.

Diagnosis

History:

- ❖ Developmental milestones & voiding history.
- ❖ Drinking & sleep habits.
- ❖ Stressful conditions.
- ❖ Symptoms of UTI.
- ❖ Symptoms of DM or DI.

Examination:

- ❖ Swelling in the back.
- ❖ Neurological examinations.
- ❖ External genitalia for congenital anomalies.

- ❖ UT examinations.

Investigations

- ❖ Urine analysis: for pus cells, glucose, specific gravity.
- ❖ Stool analysis: parasitic ova.
- ❖ Pelvi-abdominal & post voiding sonar.
- ❖ IVP
- ❖ X-ray lumbo-sacral spine.
- ❖ Voiding cystourethrography.
- ❖ Urodynamic study.

Treatment

1. Training & advices:

- ❖ Behavior modification.
- ❖ Fluid intake program.
- ❖ Bladder training (hold urine during day).
- ❖ Frequent voiding before sleep.
- ❖ Awakening child for voiding.

2. Psychiatric management: of child & parents.

3. Arousal systems:

4. Drugs:

- ❖ Antibiotics if UTI.
- ❖ Anticholinergics.
- ❖ Tricyclic antidepressant.
- ❖ ADH.

INFANT FEEDING

A balanced diet should contain

1. Protein = 15 % “ High biological value”
2. Fat = 35% “Essential fatty acids
3. CHO. =50%
4. Sufficient amount of

- * Water
- * Electrolytes
- * Vitamins
- * Minerals
- * Trace element

N.B.

1gm	Protein gives	4.1 Cal
1gm	CHO gives	4.1Cal
1gm	Fat gives	9.3 Cal

Types of infant feeding

A. Breast Feeding

1. Mother
2. Wet nurse
3. Breast milk bank

B. Artificial Feeding

1. Fresh animal milks
2. Condensed & Evaporated milks.
3. Dried animal milks

C. Mixed Feeding

1. Complementary $\Rightarrow$ to complete a breast fed.
2. Supplementary $\Rightarrow$ to replace a breast fed.

Work Hard for great success

Physiology of Lactation

At Puberty

The increase in breast size occurs due to the increase of estrogens & progesterone levels.

N.B.

Adequate levels of GH, thyroxin, insulin & glucocorticoids are also important.

During Pregnancy

1. $\uparrow\uparrow\uparrow$ Size $\Rightarrow$ Chorionic somatomamotropin
Estrogens.
Progesterone.
2. Proliferation of ducts $\Rightarrow$ Estrogens.
3. Milk Secretion $\Rightarrow$ Prolactin.

After Labor

1. $\Rightarrow$ Sudden $\downarrow\downarrow\downarrow$ in level of estrogens & progesterone $\Rightarrow$ Marked $\uparrow\uparrow\uparrow$ of prolactin $\Rightarrow$ $\oplus$ Alveolar cells $\Rightarrow$ Milk secretion.
2. Suckling $\Rightarrow$ $\oplus$ Nipple & areola $\Rightarrow$ $\uparrow\uparrow\uparrow$ oxytocin $\Rightarrow$ contraction of myo-epithelial cells which line the ducts lead to ejection of milk into lactiferous ducts $\Rightarrow$ "Let down reflex".
3. When the infant is suckling from one side of the breast $\Rightarrow$ Milk may spurt from the nipple not in use. But it can be easily stopped by tapping the nipple.
4. A third reflex, Nipple erection reflex $\Rightarrow$ results from stimulation of the nipple by suckling or tactile stimulation of the nipple.
5. Various cerebral, cortical & hypothalamic conditioned reflexes which are mediated by visual & auditory stimuli or by emotions $\Rightarrow$ All these are known to affect lactation e.g Hunger cry of the infant.

Factors affecting milk production

1) Regular complete evacuation of both breasts:

⇒ This is the most important factor for maintenance of milk secretion.

- The more vigorous the suckling, the more the milk secretion.
- Continuous suckling by the infant is necessary for maintaining milk flow.
- Suckling stimulates production of prolactin & oxytocin.

2) Hormones:

Estrogens, progesterone, prolactin, oxytocin, thyroxin & growth hormone. Normal level of these hormones are essential for initiation & maintenance of lactation.

3) Maternal health, Nutrition & Diet:

Physical fitness, good nutrition & good hydration are basic requirements for adequate milk production.

4) Psychological Factors:

- The mother should have a sincere desire to breast feed her baby.
- Psychological disturbances may decrease or even abolish breast milk production.

5) Lactagogues:

- These are agents which increase milk production.
- There is no evidence that they have more than a psychological effect on the mother e.g. Helba, Halawa tehina vit B.

N.B

*°Suckling ⇒ ↑↑↑ Prolactin serum level 10 times & Feeding more than 6 times daily maintains high basal prolactin levels.
Thus early & Frequent suckling are desirable*

Concentrate you can do it

***The Following reflexes are essential
for successful breast feeding.***

**** Infant:***

- 1. Rooting reflex.*
- 2. Suckling reflex*
- 3. Swallowing reflex.*
- 4. Satiety reflex.*

**** Mother:***

- 1. Nipple erection reflex.*
- 2. Milk secretion reflex.*
- 3. Milk ejection reflex*

Breast Feeding

Advantages

A: To the infant:

1. It is biochemically the most suitable product for infant feeding

⇒ It contains the various elements required for nutrition in the proportions optimal for digestion, absorption & body needs" i.e. perfectly balanced".

2. Naturally stored at a suitable temperature & naturally sterile.

3. Available whenever needed & automatically adjusted to infant needs.

4. It has anti-infective properties: Contains secretory antibodies (mostly IgA), lactoferrin, macrophages, lymphocytes complement.

5. Contains Bifidus factors" ⇒ ⊕ Growth of "Lactobacillus bifidus" bacteria

⇒ Minimizes the intestinal colonization with other potentially pathogenic bacteria e.g. E. Coli.

6. It contains specific growth factors for the GIT, CNS & epidermis ⇒ So Breast fed infants thrive better.

7. Breast feeding has a definite psychological advantage for both the baby & mother" maternal = Infant Bonding' Which is essential for optimum emotional development of the baby.

8. It protect against allergic diseases.

9. Proper development of facial muscles.

10. Better achievement of mental development (higher IQ).

B: To the mother:

1 .Cheap

2. Less effort of preparation.

3. Suckling is associated with rapid post-partum involution of the uterus ⇒ due to vigorous uterine contractions induced by release of oxytocin.

4. Emotional satisfaction of the mother.

5. Less incidence of cancer breast.

6 .Natural contraception.

Due to inhibition of ovulation during lactation.

50% of lactating mothers do not ovulate until the child is weaned

due to high level of prolactin, which inhibits secretion of pituitary gonadotropins.

Anti-infective properties of breast feeding

A. It is naturally sterile

B. It contains various anti-microbial factors as

1. Antibodies:

Mostly IgA against bacteria & viruses.

They are specially active against:

- E-Coli.
- Shigella
- Salmonella.

So G.E. is less common with BF.

2. Cells:

Phagocytes "granulocytes & macrophages", and
Lymphocytes of both T & B types" Mostly T-cells"

3. Complement:

Which may be involved with secretory IgA $\Rightarrow$ bacteriolysis.

4. Interferon:

$\Rightarrow$ Produced by T- lymphocytes

5. Resistant factors

$\Rightarrow$ against staphylococci

6. Proteins as:

a. Lactoferrin $\Rightarrow$ which binds to iron.

b. B12- binding protein.

Thus preventing their uptake by intestinal bacteria $\Rightarrow$ Good absorption

I.B

Iron is essential for growth & multiplication of E-Coli.

Therefore lactoferrin is considered a bacteriostatic protein for E-Coli

7. Bifidus factor:

$\Rightarrow \oplus$ Growth of lactobacillus bifidus =

Thus $\Rightarrow$ inhibition of growth of other pathogenic bacteria as E-Coli.

8. Low buffering capacity of breast milk:

$\Rightarrow$ Prevents neutralization of the gastric acidity, which is a natural barrier against infections.

9. Oligosaccharides: prevents attachment of antigens to the epithelium of the GIT.

Contraindications to B.F.

Causes in the mother

A. Absolute

There is no absolute maternal contra-indications to BF except (Cancer breast)

B. Relative

1. Maternal cachectic conditions, chronic poor nutrition & debility.
2. Chronic illness of the mother until controlled e.g.
 - HF
 - Active open TB.
 - Thyrotoxicosis.
 - Nephritis.
 - DM.
3. Acute illness of the mother until controlled e.g.
 - Eclampsia.
 - Septicemia
 - Profuse hge
 - Typhoid fever
 - Malaria
4. Mental diseases e.g.:
 - Severe neurosis
 - Post-Partum psychōsis.
 - Epilepsy.
 - Except under observation or after control
5. Maternal medications that can pass with milk & harm the baby e.g.:
 - Cytotoxic drugs
 - Anti-thyroid drugs.
 - Radio-active substances.
 - Cocaine, heroin.
 - Ergotamine.
 - Lithium.
6. Local conditions of the breast e.g.:
 - a. Nipples ⇒ Retraction Inversion
Fissuring or crackling
 - b. Breast ⇒ Mastitis Abscess
7. Pregnancy
 - Not a contra-indication during the 1st 20 weeks, After that

fetal growth is marked & deficiency diseases are liable to affect all the 3 persons

↓ Mother ↓ Baby ↓ Fetus

N.B

1. Menstruation is not a contra-indication to BF.
2. Syphilitic mother should nurse her baby because the baby is highly infectious. So, the baby should never be put to the breast of any woman except his mother, which is syphilitic.
3. Tuberculous mother: Maternal CXR....If abnormalisolate the baby till sputum examination is done.....If +Ve...INH is given to the baby till sputum of the mother is negative for 3 months then Do tuberculin test to the baby..... if +Ve continue INH for 9-12 months..... if -Ve INH can be stopped.
4. Maternal rubella is not a contraindication.
5. Maternal herpes simplex is a contraindication only if there is active lesions near the nipples.
6. Maternal hepatitis B during pregnancy is not a contraindication if the infant receives at birth hepatitis B vaccine & specific hepatitis B Igs injected at different sites. If the mother acquired infection during nursing the infant should receive accelerated vaccination (0, 1 & 2 months).
7. Maternal AIDS: transmission via breast milk is well documented & is a contraindication if there is a safe alternative.

Causes in the infant

A. Absolute:

Inborn Errors of Metabolism ~ IEM" as phenylketonura "PKU", galactosemia & lactose - intolerance ⇒ Breast milk & Animal milks are hazardous & special types of artificial milk are indicated.

B. Relative:

1. Acute illness of the infant

⇒ in these conditions breast milk can be expressed & given to the baby by a spoon or dropper, because BF is too tiring for him.

The same can be done in the presence of congenital anomalies e.g. cleft lip & palate.

2. Breast milk jaundice

⇒ due to presence of 3α . 20- β pregnandiol in breast milk, which is a metabolite of the progesterone ⇒ inhibition of glucuronyl transferase

enzyme which is responsible for conjugation of indirect bilirubin to direct bilirubin

TTT ⇒ stop BF for only 48 hrs then continue it again.

Difficulties in BF

Obstacles in the mother

A. Delayed milk production

As in cases of C.S. & traumatic shocky labor or any cause that delays suckling.

TTT ⇒ If there is marked delay we usually resort to complementary feeding & the baby should suckle the breast first in every fed.

B. Developmental abnormalities

1. Absent or small breast

⇒ give complementary feeding

2. Pendulous breast

⇒ Support the breast during feeding.

3. Absent, small or flat nipples

⇒ If it occurred, breast milk can be expressed & given to the baby. Artificial nipple or breast pump may be used.

C. Painful conditions of the breast

1. Acute milk engorgement

It is painful conditions of the breast occurs in 2nd or 3rd day after birth.

It is due to inadequate suckling of the breast with milk.

The condition can be prevented by regular & complete evacuation of the breast.

Severe conditions can be managed (Parlodel) & stopped when the condition is improved.

Suckling should not be stopped.

2. Mastitis & Breast abscess

⇒ Regular artificial evacuation of the affected side should be done + Antibiotics + hot fomentations

* If abscess is formed ⇒ drainage.

3. Fissuring & Cracking of nipples

These can be prevented by:

a. Local cleaning using bland water.

b. Prevent breast engorgement

- c. Prevent prolonged useless suckling.
- d. Keep the nipple dry.
- e. Application of lanolin, panthenol creams enhances healing..

Obstacles in the baby

1. Congenital Anomalies: Cleft lip, Cleft palate micro-gnathia, esophageal atresia, CHD. Etc.
2. Nasal obstruction: bilateral choanal atresia, adenoids, common cold.
3. Painful conditions of mouth: Stomatitis. Oral moniliasis, ulcers & Natal teeth.
4. Birth trauma
5. Prematurity.
6. Pneumonia & other causes of RD
7. Irritable neurotic infants.

Instructions for BF

- * We should explain to every mother the variable advantages of breast feeding over other methods, in addition to the various factors that affect milk production & difficulties of BF
- * A mother willing to breast fed her baby is the key for success.
- * The following instructions are a possible guide to the lactating mother.

I. Initiation of Feeding:

- Should be started as soon as the mother recover from fatigue of labor.
- This is usually within the 1st 6 hrs after labor.
- The baby is put to each breast for about 1-3 mm then the duration is gradually ↑↑

II. Technique of feeding

1. The mother should be sitting in a comfortable position.
2. The nipple & areola should be clean using fresh water "Don't use detergent soap".
3. The baby is hold in a semi-recumbent position on mother's arm, and the breast is held by the index & middle finger of the other hand, with mild gentle squeezing using the thumb.
4. Both breasts should be used at the same fed initially.

- Later on, if milk supply is adequate $\Rightarrow$ Alternate breasts should be used at each fed.
 - If one breast doesn't satisfy the baby $\Rightarrow$ both breasts used first at one fed should be used second at the next fed.
 - It is advised to exhaust one side before shifting to the other breast, because the fat content in the last portion of the fed is higher.
5. At the middle & again at the end of the fed the infant should be raised to a sitting position or held in the erect position to allow air swallowed during suckling to escape from the stomach "Eructation" Why? $\Rightarrow$ to prevent regurgitation of milk.
 6. After feeding, the baby is better put in the prone position, with his face to one side to prevent aspiration if regurgitation occurs.
 7. Boiled water "allowed to cool" may be given to the baby at any time, especially in hot weather.
 8. If supplementary or complementary feeding is needed, care should be taken that only unsweetened milks should be used $\Rightarrow$ because the baby may like it & refuse breast milk.
Also the holes in the bottle teat should not be too wide making it more easy than breast feeding.

III. Duration of feeding

N.B Initially, the time of suckling is limited to 1-3 min on each breast, on the 1st day. This period is gradually increased until it is 5-10 minutes on each breast.

1. The baby should not be allowed > 20 minutes / fed $\rightarrow$ Why?
2. Most milk is taken from the breast in the 1st 5 minutes & the baby is often satisfied after 10 minutes

IV. Frequency of feeding

2 methods are used .

A. Demand method

A. Demand method

Which is self regulatory method. The feeding started when the baby cries from hunger.

Recently, considered as the best method as it allows him to physiologically regulate his intake. However, it should be noted that all crying is not due to hunger, but it may be due to thirst, soiling colic, cold or a demand for attention should be looked for.

B. Regular O'clock method

B. Regular O'clock method

The usual schedule is at 3 hourly interval starting at 6 AM till 9 PM, with an additional midnight feeding in the 1st 2 months.

N.B

The frequency of feeding is decreased with age e.g.

- 1) 1st 4 months $\Rightarrow$ Every 3hrs = 6-7 feeds / D
- 2) 4th 10th month $\Rightarrow$ Every 4 hrs = 5 feeds / D
- 3) 10th - 12th month $\Rightarrow$ Every 5 hrs = 4 feeds / D

* *The 4 hourly feeding program is indicated in*

- 1) Over — weight baby.
- 2) Liberal breast — milk supply
- 3) After the age of 4 months.

* *The 2 hourly feeding program is indicated in*

- 1) Premature & under weight.
- 2) Scanty breast milk supply.

The Efficiency of milk Supply

This can be evaluated by the following points:

1. The baby looks satisfied after feeding & goes into sleep.
2. Proper gain in weight.
3. No. of stools $\rightarrow$ constipation = under feeding.
 $\rightarrow$ Diarrhea = overfeeding.

4. Test Feed:

- Weighing the baby before & after each fed for 3 successive days.
- The average increase in wt / feed is then calculated.
- If the average is less than the amount supposed to be taken by the baby $\Rightarrow$ the cause should be searched for; either in the mother or in the baby.
- To differentiate between these, express the breast after each feeding

If no milk is present

Scanty milk production

if milk is present

obstacles in the baby

5. +ve Let down reflex" Milk-ejection Reflex" $\Rightarrow$ Appearance of milk in the other breast during suckling is a good indicator of efficient milk production.

6. Chemical analysis of milk for its protein, CHO & lipid content.

Under Feeding

Etiology

I. In breast fed infants

⇒ the cause is either in the infant or in the mother "see obstacles of breast feeding".

II. In artificially fed infants

⇒ the cause is either insufficient amount of milk, or too diluted concentration of the formula.

C / P

1. The infant is not satisfied after feeding, doesn't go into sleep, always crying before and after feeding, & suckling his fists between feeds (hunger).
2. Failure to gain weight, then loss of weight.
3. Constipation, with few small & hard stools.
4. Oliguria + signs of dehydration.
5. Pallor
6. Test feed.
⇒ below normal

t t t

1. In breast fed infants

⇒ t t t of the cause.
+ complementary feeding.

2. In artificially fed infants

⇒ Correction of both the quantity & quality of the formula.

Over - Feeding

Etiology

I. In breast fed infants.

1. ⇒ Frequent feeding
2. ⇒ prolonged nursing time.

II. In artificially fed infants

1. → Concentrated formula
2. → Excessive amount

C/P

1. Vomiting esp. after feeding & crying due to colic & flatulence
2. Over-weight infants.
3. Diarrhea with large bulky & offensive stools.
4. Polyuria + sore buttocks.
5. Test feed ⇒ Above normal.

t t t

I. In breast fed infants.

- ⇒ Regulation of feeding &
Limitation of nursing time to 20 minutes.

II. In artificially fed infants

- ⇒ Correction of both quantity & Quality of feeding.

Stages of Milk Secretion

A. Colostrums

- ⇒ For 2-4 days after delivery

B. Transitional milk

- ⇒ 5-20 days after delivery

C. Mature milk " fully established

- ⇒ 3 weeks after delivery.

Colostrums

Definition

It is the secretion of the breast during the 1st 2-4 days after birth. This secretion may start few days before birth.

Character

1. Color $\Rightarrow$ Yellowish (β -Carotene).
2. Reaction $\Rightarrow$ Alkaline.
3. Specific gravity $\Rightarrow$ 1040
4. Amount $\Rightarrow$ Varies between 2 & 20 ml / feeding during the 1st 3 days, then it increases & can be as high as 100 ml.

Compositions

1. Protein $\Rightarrow$ 2.7 gm /dl
2. Fat $\Rightarrow$ 2.9gm /dl(It has less total fat & higher cholesterol which gives it the yellow color than mature milk).
3. CHO $\Rightarrow$ 5.3 gm /dl (It has less lactose than mature milk).
4. Ash $\Rightarrow$ 0.5 gm /dl (the concentrations of Na, K & Cl are greater than those of mature milk).

Microscopic Picture

1. Colostrums corpuscles, lymphocytes, PMNL & Fat globules
2. The colostrums corpuscles disappear normally with establishment of mature milk.

N.B

• Persistence or reappearance at any time during lactation is an indication that milk production will stop.

Advantages

1. Highly nutritive.
2. Suitable composition.
3. High Antibody content "esp. IgA" & Leukocytes.
4. Better involution of birth canal $\Rightarrow$ due to early suckling.
5. Natural laxative effect : It facilitate passage of meconium because of high oligosaccharide content..

Mature Breast Milk

Characters

- | | |
|-----------------------|-----------------------|
| 1. <u>Color</u> | $\Rightarrow$ White |
| 2. <u>Consistency</u> | $\Rightarrow$ Thin |
| 3. <u>Reaction</u> | $\Rightarrow$ Neutral |

- | | |
|----------------------------|--|
| 4. <u>Specific gravity</u> | $\Rightarrow$ 1030 |
| 5. <u>Amount</u> | $\Rightarrow$ up to 1-2 Liters /D |
| 6. <u>Microscopically</u> | $\rightarrow$ small, fine, fat globules. |
| 7. <u>Caloric value</u> | $\Rightarrow$ 67 cal / 100 ml |

Composition

A. Quantitative

1. Water $\rightarrow$ 88 %
2. Solids $\rightarrow$ 12 %
3. Calories $\rightarrow$ Each 100 ml supply 67 cal.
 $\quad\quad\quad$ "150 ml = 100 cal. Or 3ml = 2 cal".
4. Protein $\rightarrow$ 1 - 1.5 gm/dl
5. Fat $\rightarrow$ 3.5 gm /dl.
6. CHO $\rightarrow$ 7gm /dl
7. Ash $\rightarrow$ 0.25 gm /dl

B. Qualitative

1- Proteins:

- Composed of
 - a. 60% are soluble "lactalbumin + lactoglobulin"
 - b. 40% are insoluble "caseinogen"
- Casein curd in human milk is fine, thin & easily digested.
- Contains all the essential A.A. in suitable proportion, including "Taurine" which is essential in low birth weight.
- It has lower phenylalanine, tyrosine & methionine level (newborn has lower levels of enzymes necessary for their metabolism).
- It is rich in cystine.
- Other important breast milk proteins:
 - a. Lysozymes.
 - b. Lactoferrin.
 - c. Immunoglobulins, hormones & hormones.
 - d. Zinc & copper binding proteins & transferring.
 - e. Epidermal growth factor.

2. Fat:

- Small size of fat globules.
- Small amounts of volatile F.A. "only 1.3% of total".
- High percentage of essential F.A. "Poly-unsaturated F.A. = 8% of total fat"

- The lipid content of breast milk varies according to many factors. e.g. within the feed (the hind milk has more fat than fore milk), stage of lactation, weaning, diurnal rhythm & gestational age at birth.
- They contain lipase (facilitate digestion of fats).
- They contain cholesterol which is essential for brain growth, bile acid & hormonal synthesis.
- They contain Omega-3 long chain fatty acids which is essential for brain development.

3. CHO:

- Beta – lactose is the only CHO of milk.
- Lactose is specific for newborn growth. It enhances Ca & iron absorption, so it has a role in prevention of rickets & iron deficiency anemia.
- Lactose favors the growth of lactobacillus bifidus which gives lactic acid which decrease growth of E-coli.
- Lactose is the source of galactose that is essential for production of galactolipids which is essential for brain growth.
- Oligosaccharides decrease the incidence of infection....see before.

4. Minerals:

- Ca : Ph ratio is 2:1 which is optimal for absorption (about 70 % of it absorbed while 25% of Ca absorbed from cow milk)..So hypocalcemia & tetany is more common in cow's milk fed infants.
- Cow's milk also has higher phosphorus concentration that impair Ca absorption.
- Iron & Copper are deficient. But in spite of this, its biological availability for absorption is high, So no deficiency occurs in breast fed infants in the 1st year.
- Breastfed infants do not have the risk of iron loss, as do infants fed cow's milk because they may have microhemorrhages of the bowel as a result of mucosal damage by non human milk.
- Early introduction of solid food impair iron absorption from breast milk.
- Iron supplementation is usually not needed for breastfed in the 1st 6 months.
- Excess iron will saturate lactoferrin & diminish its anti-infective properties.
- Zinc is essential as an enzyme activator. Its level in breast milk

rise to peak level in the 2nd day.

- Zinc requirements are relatively high in the very young infant & decrease as the infant's age increases.

5. Vitamins:

- As lactation progresses, the level of water-soluble vitamins increases & the level fat-soluble vitamins decrease.
- Vit-A are present in an adequate amounts & it is main source of vitamin-A in developing countries even after the 1st year of life.
- It contains inadequate amount of Vit- C,D,K.
- Human colostrums & mature milk are rich in vitamin E., it is an antioxidant; so it protects all membranes in the retina & lungs against oxidant induced injury.
- Vitamin E deficiency will cause hemolytic anemia, especially in premature infant.
- Early ingestion of breast milk enhances growth bacterial flora which produce vitamin K.

6. Buffer Value:

Human milk has a lower buffer value than cow milk, thus it is easily digested because it doesn't need high gastric acid.

Comparison between human & Cow milk

	<i>Human milk</i>	<i>Animal milk</i>	<i>Formula</i>
<i>Protein</i>	Correct amount easy to digest	Too much difficult to digest	Partly corrected
<i>Fat</i>	Enough essential FA, lipase to digest	Lacks essential FA, no lipase	Lacks essential FA. no lipase
<i>Vitamins</i>	Enough	Not enough A & C	Vitamins added
<i>Minerals</i>	Correct amount	Too much	Partly corrected
<i>Iron</i>	Small amount well absorbed	Small amount not well absorbed	Extra added not well absorbed
<i>Water</i>	Enough	Extra needed	May need Extra
<i>Anti-infective</i>	Present	Not present	Not present
<i>Growth factors</i>	Present	Not present	Not present

Q: How can you alter the casein in animals milk?

1. Boiling.
2. Dilution with water
3. Acidification.
4. Drying or condensation.

Calculation of the amount of milk needed

Age method "Rule of Tens"

- 1st day → 10 ml / fed.
1st week → ↑ 10 ml / fed each day.
1st Month → ↑ 10 ml / fed each week.
1st Year → ↑ 10 ml / fed each month.

During the 1st year of life the following equation is used ⇒

$$\text{Amount of milk / fed} = (\text{Age in months} \times 10) + 100$$

Weight method

$$\text{Amount of milk / fed} = (\text{Wt "Kg"} \times 20) + 20$$

Caloric method

- The total caloric needs of the infant per day are calculated, then the volume of milk containing this amount is calculated.
- This volume is then divided by the number of feds.

N.B

- This is 'the most accurate method esp. during disease & malnutrition.

Artificial Feeding

Indications

1. Contra-indications of breast feeding.
2. Absent mother "death, travel, work, etc."
3. As complementary or supplementary feeding.
4. In feeding of twins.
5. Particular diseases : PKU, Galactosemia, lactose intolerance, HF, Nephrosis.

TYPES

A. Fresh animal milk.

B. Evaporated & condensed sweetened milks.

C. Dried milks.

1. Cream milk ⇒ full cream
Half cream
Skimmed milk
2. Acidified milk ⇒ Full cream
Half cream
Skimmed
3. Humanized milk
4. Protein milk
5. Special types of milk
 - Hypo- allergenic milk
 - Salt-free milk
 - Lactose - free milk
 - Phenyl- alanine free milk
 - Premature milk Formula.

Fresh Animal Milk

When fresh animal milk is used for infant feeding the following points should be considered:

1. Calculate the amount of each fed.
2. No. of feds / day.
3. Modifications of milk to approximate human milk "Humanization"
4. Sterilization of milk ⇒ by boiling for 15 minutes or by pasteurization, which is heating at 62°C for 1/2 hr then rapid cooling ⇒ This kills most of the bacteria.

Q: How to humanize buffalo milk?

- This is done by dilution of milk by water in 1: 1 ratio, and addition of 6 gm sucrose /dl & boiling of the milk.
- This approximates its composition to that of human milk, regarding the protein & caloric contents.
- Moreover, dilution & boiling help to modify the casein curd, rendering it less tough & more easily digested.
- Also, the fat contents is lowered, and the fat globules are rendered' smaller. So they are more easily digested.

Composition	Buffalo	After Humanization	Human
Protein "gm/dl"	4	2	1.2
Fat "gm/dl"	6	3	3.5
CHO "gm/dl"	4	2.6 gm sugar	7
ash "gm/dl"	0.9	0.45	0.25
Calories / dl	100	67	67

Evaporated & Condensed Sweetened Milks

- These are made of cow milk after being concentrated.
- In sweetened milk sucrose is added in a high concentration.
- They are usually used by adults not by infants.

Advantages

1. Alteration of casein.
2. Can be kept sterile for long periods.

A. Evaporated milk

⇒ is prepared by dilution
1: 5 in water.

B. Condensed milk

⇒ is prepared by dilution 1 : 5 in water.

Dried Milks

Methods of preparation

1. Roller method
2. Spray method

Advantages

1. Sterile & easily stored.
2. Easily handled & can be prepared fresh for every fed.
3. Constant in composition.
4. Drying renders the curd softer & smaller.
5. Can be fortified with vitamins & minerals.
6. Different types are available for different ages & diseases.

Types

A. Cream Milks

I. Full cream: fat content 4 gm%

Indication:

1. Completely healthy infants over 4 months age.
2. In cold weather because of high caloric contents.

e.g. Nestogen full cream

II. Half cream: Fat content 2-3 gm%

Indication:

Healthy infants less than 4 m.

e.g. Bebelac Z12.

III. Skimmed milk: Fat content 0.5-1 gm% (not available)

Indication:

1. Fat intolerance & malabsorption.
2. Convalescence from diarrhea .
3. Prematurity.

B. Acidified Milks:

Methods of acidification

1. Chemical $\Rightarrow$ lactic acid.
2. Biological $\Rightarrow$ by fermentation using lactobacillus acidophilus or lactobacillus bulgaricus.

Advantages.

1. Easily digested $\Rightarrow$ Why?
2. Casein is altered into fine curd.
3. Acidity enhances Ca^{2+} absorption.
4. Disinfectant effect on GIT
5. Shorter stay in stomach $\Rightarrow$ So it is indicated in cases of vomiting.

Indications:

1. Infants with digestive troubles.
2. Recovery from diarrheal diseases.
3. Premature & Low birth weight.
4. Protein calorie malnutrition.
5. Habitual vomiting.

TYPES

1. Acidified full cream
2. Acidified half cream.
3. Acidified skimmed.

N.B

- Skimmed milks have low caloric content (Low fat).
So, not suitable for prolonged periods.

C. Humanized Milks

The following modifications have been done:

1. Proteins, CHO, fat have been roughly approximated to human milk.
2. Protein is modified to form soft, small curd to be easily digested.
3. Mineral content is lowered to approximate human NaCL content, while Ca/p ratio is optimized to be 2/1
4. Vitamins & Iron are sometimes added to fortify milk.

Indications: In Feeding of healthy infants

e.g. Similac, SMA, S26, Enfamil NAN, Bebelac I.

Protein Milk:

- This is prepared by addition of dry casein to Butter milk.
- It has a low CHO & low caloric value.

Composition:

- | | | |
|------------|---|--------|
| 1. Protein | ⇒ | 5 gm |
| 2. CHO | ⇒ | 3.5 gm |
| 3. Fat | ⇒ | 2.5 gm |

It can not be used for a prolonged time due to.

1. It's bad taste.
2. Causes constipation.
3. Expensive.
4. Has low caloric value.

Indications

1. Diarrheal diseases.
2. Debilitated infants.
3. Preterm babies.

N.B

It is prepared by addition to rice water or an adapted or any special formula .

Special types:

1. Hypo-allergenic milks (vegetable milk).

- Indicated in: infants allergic to human & animal proteins, Lactose intolerance & galactosemia.
- Vegetable protein "Soya protein " is used to replace the milk protein & the lactose of milk is replaced by other sugar (Sucrose or glucose) e.g. Nursoy, Isomil.

2. Salt – Free milks

Indications

1. HF
 2. Congenital Nephrosis.
 3. Steroid therapy.
- e.g. Lonalac

3. Lactose Free milks

Indications

1. Galactosemia.
2. Lactose- intolerance.
e.g. Isomil

4. Phenyl-alanine free milks

Indications:

- ⇒ PKU
e.g. Lofenalac

5. Premature milk formula.

Contains 80 Cal / dl

It is used to promote & support increased nutritional needs of the premature baby.

e.g. Pre NAN, Enfamil LBW.

6. Predigested milk (elemental):

Indications:

- Intractable diarrhea.
- Protein losing enteropathy.
- Malabsorption due to pancreatic & biliary insufficiency.

In these formula the protein is present in the form of amino acids; fat in the form of medium chain triglycerides & CHO in the form of glucose polymers. '

Disadvantages:

- a. Bad taste.
- b. Constipation.
- c. Expensive.

Weaning

Definition

Addition of solid & semisolids foods other than milk to the feeds of the baby.

Time of weaning.

Usually started at the age of 4 months to be complete at 1-2 years. After the age of 4 months. Milk is not a sufficient diet for the infant.

Addition of new food should be postponed in the following conditions.

1. In very hot weather.
2. Convalescence from any disease.
3. Following G.E.
4. During eruption of new tooth.

Principles of weaning.

1. Added food should be initially nearest in composition & taste to milk as pudding & yogurt.
2. Any new food should be offered initially once a day in small amounts until the whole feed is replaced.
3. Attractive plates & colorful arrangement to stimulate the babies interests.
4. Foods should be sieved strained or pureed at the start of weaning "thin consistency.
5. Feeds should be freshly prepared "for fear of contamination.
6. Additions should be tried separately i.e. no more than one new food should be given at a time week.
7. Additions should be given at a fixed time of the day. This helps the development of the conditioned reflexes of GIT.
8. If the baby dislike the new food, $\Rightarrow$ it should be omitted and tried in another occasion, some weeks later.
9. The first feed to be replaced is the mid-day fed & the last feed to be replaced are the 1st & last. They should stay milk to the end of weaning.
10. Additions should be given with a spoon or with cup.
11. It should be emphasized that there's no strict rules for weaning However this principles help to perform a successful program.

Nutritional Disorders

Adequate Diet

It should fulfill the following criteria:

1. Adequate total calories.
2. Adequate proportions of protein, fat & CHO.
3. Adequate amount of vitamins & minerals.
4. Adequate amount of water.

Balanced diet

It should contain adequate proportion of fat, CHO & proteins:

1. CHO $\Rightarrow$ 50 %.(1 gm = 4.1 Cal).
2. Fat $\Rightarrow$ 35 % (the main source of energy , 1 gm = 9.3 Cal).
3. Proteins $\Rightarrow$ 15 %.(1 gm = 4.1 Cal)

How to calculate the caloric requirement for normal child ?

Premature: 120 Cal / Kg / day.

Newborn: 100-120 Cal / Kg / day.

Children:

- 1st 10 Kg $\Rightarrow$ 100 Cal / Kg / day.
- 2nd 10 Kg $\Rightarrow$ 50 Cal / Kg / day.
- Over 20 Kg $\Rightarrow$ add 20 Cal / Kg / day.

Ideal diet

1. Adequate diet.
2. Palatable.
3. Available.
4. Cheap.



Come on .. Do your best

Abnormal Nutrition

Under-nutrition

Due to deficiency in the total caloric supply as well as deficiency in the 3 basic food stuffs (CHO – fat – proteins) & deficiency of minerals & vitamins e.g. marasmus.

Malnutrition

Deficiency or excess of one or more of the food stuffs with almost normal total caloric supply.e.g.

1. ↓↓↓ Vitamin D $\Rightarrow$ Rickets.
2. ↓↓↓ Proteins $\Rightarrow$ KWO.
3. ↓↓↓ Fe $\Rightarrow$ iron deficiency anemia.
4. ↑↑↑ Calories $\Rightarrow$ obesity.
5. Hypervitaminosis.

Mixed malnutrition & under-nutrition

There is deficiency of one or more of food stuffs + deficiency of total caloric supply e.g. marasmic KWO.

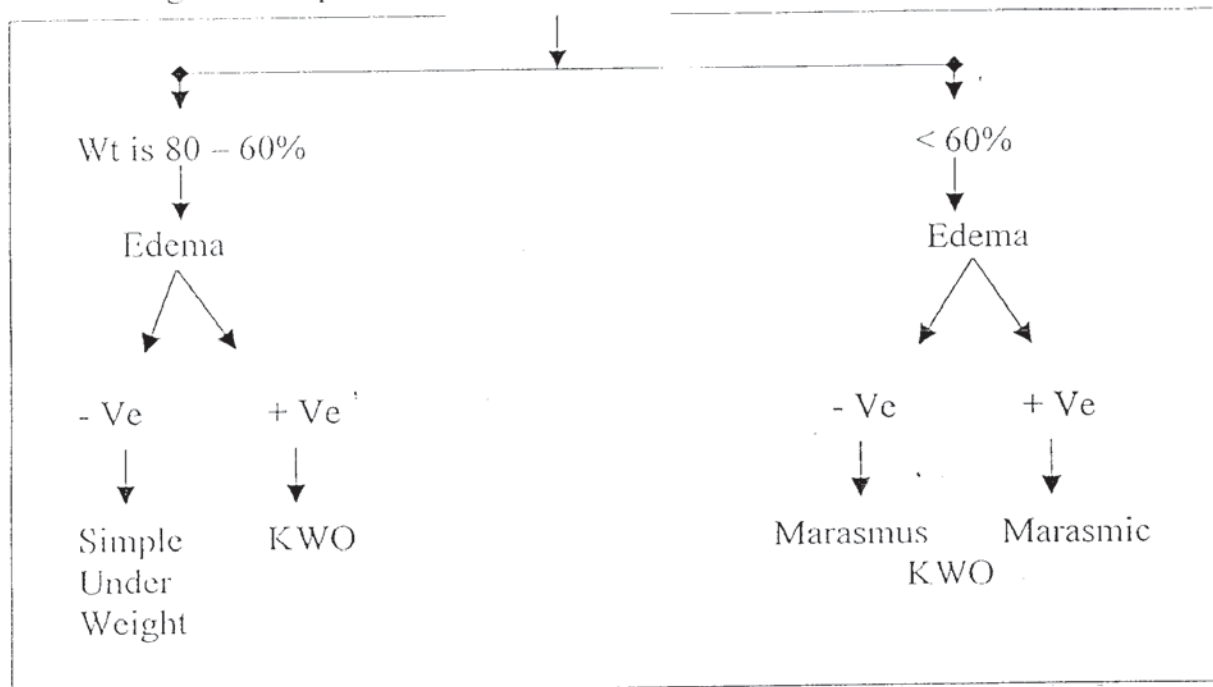


Work hard .. It's great challenge

Classification of Nutritional Disorders

Wellcome Classification 1970

Protein - Energy Malnutrition " PEM" is classified according to the weight of the patient in relation to its age as follows



Marasmus "Infantile Atrophy"

Definition

It is a state of chronic under-nutrition in the form of deficiency of total caloric supply as well as deficiency of different food stuffs. It is characterized by progressive loss of weight reaching below 60 % of the normal.

Etiology

I. Dietetic Errors (1ry marasmus):

A. Quantity

1. Scanty breast milk.
2. Small amount of feed
3. Widely spaced feeds
4. Delayed weaning.

B. Quality

1. Diluted formula in artificial feeding.
2. Cow-milk protein allergy.

C. Nursing Errors

1. Irregular feeding
2. Air-swallowing with failure of eructation.

D. Feeding difficulties:

1. *Breast fed*: in both baby & mother.
2. *Artificial fed*; in the baby only.

E. In weaned infant:

Failure to maintain well balanced diet.

II. Non dietary causes (2ry marasmus)

1. Infections:

- GE (the commonest) only if prolonged or recurrent.
- TB.
- Chronic chest infections.
- Chronic suppurative otitis media.
- Urinary tract infection.
- Congenital infections.

2. GIT causes:

a. Congenital:

- Cleft lip & palate.
- Congenital hypertrophic pyloric stenosis.

b. Malabsorption syndromes

3. Chronic systemic disorders:

- a. Congenital heart diseases.
- b. Recurrent or intractable heart failure.
- c. Renal tubular acidosis.
- d. Obstructive uropathy.
- e. Chronic renal failure.
- f. Congenital lung cysts.
- g. Hepatic cirrhosis.
- h. Severe mental retardation.
- i. Neurological deficits e.g. palatal paralysis.

4. Prematurity

Due to

1. Weak suckling
2. Poor absorption
3. Poor stores
4. High caloric needs/Kg

5. Metabolic Diseases

1. Glycogen storage disease.
2. Galactosemia.
3. Phenylketonuria.



6. Endocrine Diseases

1. Thyrotoxicosis.
2. D.M.

7. Chromosomal disorders.

Pathology

Defective total caloric intake $\Rightarrow$ utilization of spare tissues (hepatic glycogen & fat) for energy production

Persistence of the condition $\Rightarrow$ utilization of fixed tissues (proteins in the muscles & organs) $\Rightarrow$ Picture of generalized atrophy

1. *Loss of hepatic glycogen.*
2. *Loss of sub-cutaneous fat*
3. *Atrophy of muscles & other internal organs*
4. *Bones $\Rightarrow$ Osteoporotic "Atrophic-rickets"*

C/P

C/O

The usual C/O is failure to thrive

But it may be presented by one of the complications or etiological factors.

History

1. History of growth delay. "developmental history"
2. History of nutritional troubles "Dietetic history"
3. History of one of the etiological factors or complications.

O/E

1. Growth failure

- First there's failure to thrive $\Rightarrow$ Followed by progressive loss of wt.
- This can be detected early from the growth curve of the baby.
- According to wellcome classification the wt is less than 60% of expected.

2. Loss of S.C. Fat

- There's marked loss of S.C. fat $\Rightarrow$ $\downarrow\downarrow$ Skin fold thickness.
- The skin becomes thin & wrinkled esp. at the flexural areas.

- According to its distribution marasmus can be

Senile face
"3rd degree"

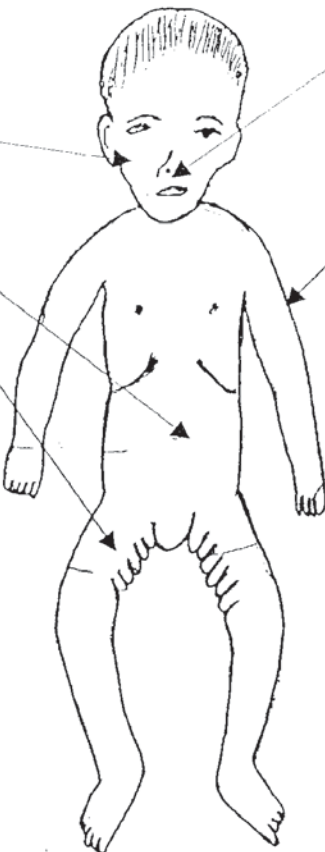
Abdominal Wall
"1st degree"

Limbs & buttocks
"2nd degree"

3. Muscle Wasting

↓
marked prominence of bony surfaces

↓
The whole picture is that of skin over bone



4. Marked pallor

5. Mid-arm circumference

↓
The marked atrophy of ms. & S.C. Fat ⇒ ↓↓ midarm circumference

N.B.

- Normally at the age of 1 year ⇒ > 13.5cm

- In early cases = 12.5 - 13.5 cm

- In full marasmic pts = < 12.5cm

6. Skin manifestations:

- Loss of skin elasticity.
- Skin is thrown into multiple folds especially at the groins.
- So we can not depend on loss of skin elasticity as a sign of dehydration in marasmus

7. Abdomen:

- Scaphoid abdomen due to thin abdominal muscles.
- Visible peristalsis due to thin abdominal muscles.

8. Irritability: due to hunger pains.

9. Hypothermia: due to :-

- a. ↓↓↓ Caloric intake.
- b. Loss of S.C.fat ⇒ increase heat loss.
- c. ↓↓↓ Muscle bulk ⇒ impaired shivering.
- d. Dehydration & electrolyte imbalance.
- e. Septicemic shock.

10. GIT manifestations

- The patient is always hungry, but anorexia is present in advanced cases.
- Constipation $\Rightarrow$ may be present due to decrease food intake.
- Diarrhea $\Rightarrow$ due to

1. G.E.
2. Maldigestion
3. Malabsorption (commonly lactose intolerance).
4. Starvation diarrhea.

N.B.

Starvation diarrhea is common

- Characters

1. Small amounts
2. Loose
3. Dark in color
4. Offensive odor

- It is composed of

1. Cellular debris.
2. Greenish mucus.
3. Intestinal flora.

11. CVS:-

- Weak & slow pulse.
- In case of dehydration $\Rightarrow$ weak & rapid pulse.
- Peripheral circulatory failure is the end stage.

Marasmus

12. Respiratory system:-

- Shallow respiration $\Rightarrow$ due to weak respiratory muscles.
- Repeated chest infection.

13. Signs of mineral & vitamin deficiency $\Rightarrow$ see later.

14. Inter-current infections (due to impaired immunity)

1. G.E.
2. Bronchopneumonia "Main cause of death"
3. O.M.
4. Urinary tract infections
5. T.B.

Investigations

Marasmus is a clinical diagnosis, but we need investigations for diagnosis of the cause & complications if present.

1. Stools:

- Parasites
- Steatorrhea

- Malabsorption.

2. Urine:

- Culture & Sensitivity
- Sugar & Ketones $\Rightarrow$ DM
- $\uparrow\uparrow$ Urea due to hyper-catabolism of proteins.

3. CBC

- Anemia $\Rightarrow$ see KWO later.
- $\uparrow\uparrow\uparrow$ Total & differential WBCs due to infection.
- $\uparrow\uparrow\uparrow$ ESR due to infection.

4. Chemistry:

- Slight hypoproteinemia.
- $\uparrow\uparrow\uparrow$ Igs due to infections.
- Fasting hypoglycemia.
- Serum electrolytes may be disturbed due to GE & dehydration.

5. CXR

- Congenital heart disease
- T.B.
- Bronchopneumonia.

6. Tuberculin test $\Rightarrow$ For T.B.

7. Intestinal biopsy.

8. Estimation of digestive enzymes

Complications

1. Intercurrent infections

2. Hemorrhagic tendency & purpura It is a bad sign.

It is due to:

- Loss of SC support of blood vessels.
- DIC due to severe dehydration & fulminant infection.

3. Edema $\Rightarrow$ Marasmic KWO if the patient is fed on CHO diet with deficient protein.

4. Hypothermia

5. Hypoglycemia due to lack of glycogen stores in the liver.

6. Dehydration & electrolyte imbalance, acid base disturbances & shock.

7. Peptic ulceration.

Kwashiorkor KWO

Definition

It is a clinical syndrome which results from malnutrition in the form of deficient protein intake with adequate total caloric intake through a CHO diet.

- So, it is called **Protein Energy Malnutrition**

N.B.

◦ It is also called the disease of deposed baby because it usually affects the elder baby when the next is born (i.e. Maternal deprivation).

Epidemiology

- Mostly at the age of 6 ms -3 Years following & coincident with weaning
- Rare < 6 months.
- Never > 3 years because he can struggle for eating.
- Common in low socio-economic class.

Etiology

- Primary KWO (Dietetic)
 - Unbalanced diet, with minimal protein intake & high CHO intake.
 - This is common to occur at the time of weaning.
 - Also, faulty management of marasmic babies, by giving them a CHO diet only will result in marasmic-KWO.
- Secondary KWO:
 - Resulting from other diseases, which are usually predisposing factors rather than actual causes as these diseases will lead to:
 1. Anorexia & stomatitis.
 2. Malabsorption & protein losing enteropathy.
 3. Prolonged dietary restriction e.g.
 - a. GE.
 - b. Whooping cough.
 - c. Measles.
 - d. Parasitic infestation.

C/P

<i>Essential Features</i>	<i>Variable features</i>
1. Growth retardation 2. Edema 3. Mental changes 4. $\downarrow\downarrow$ Ms / fat ratio	1. Hair changes 2. Skin changes 3. Hepatomegaly 4. GIT troubles 5. Vitamins & mineral deficiency 6. Anemia 7. Infections

I. Growth retardation

- Early, there is slow rate of growth when measured on growth curves.
- The wt is affected $>$ height
- The wt is usually 60-80% of the expected.
- The loss of weight may be masked by edema & excess SC fat.
- In advanced cases bone age may be delayed.

II. Edema

It is characterized by

1. Pitting
2. Site: starts in the dorsum of the hands & feet then spreads centrally, to involve legs, arms, face & does not affect the anterior abdominal wall.
3. It never causes ascitis or effusion.

Causes:

1. Low serum albumin $\Rightarrow$ is the main cause $\Rightarrow \downarrow\downarrow$ effective plasma oncotic pressure.
2. 2ry Hyper-aldosteronism
 $\Rightarrow$ Why?
3. $\uparrow\uparrow$ ADH level $\Rightarrow$ Why?
4. Altered capillary permeability due to protein deficiency.

III. Mental Changes

These are represented by lethargy, apathy, misery, Sluggish movement, anorexia & disinterest in the surroundings.

Causes

$\Rightarrow$ Causes of brain pathology.

Pathology

I. Fatty liver $\Rightarrow$ Hepatomegaly

It never leads to cirrhosis except if the condition is prolonged.

Causes

1. Deficiency of lipotropic factors e.g. Methionine & Choline,
2. Defective formation of lipoproteins $\Rightarrow$ due to $\downarrow\downarrow$ plasma proteins.,
3. Vit- B complex deficiency.

II. Excess S.C. Fat

III. Atrophy of intestinal villi.

- $\Rightarrow$ 1. Malabsorption
2. $\downarrow\downarrow$ Disaccharidase enzymes $\Rightarrow$ Mal-digestion (commonly lactase deficiency $\Rightarrow$ lactose intolerance).

IV. Generalized muscle wasting

$\Rightarrow$ due to $\downarrow\downarrow$ protein

V. Pancreas

Atrophy of pancreatic acini

$\Rightarrow \downarrow\downarrow$ pancreatic enzymes

$\Rightarrow$ Malabsorption & maldigestion

VI. Heart

Degenerative changes $\Rightarrow$ H.F.

VII. Kidney $\Rightarrow$ Hyaline degeneration of the glomeruli & may be tubular cells.

VIII. Brain

Slow atrophy $\Rightarrow$ Mental changes

Causes

1. $\downarrow\downarrow$ Aromatic A.A. tryptophan tyrosine & phenyl -alanine which are needed for proper growth of the brain.

2. Hypothyroid function

N.B.

• Mental changes are reversible by t t t. however if the condition is severe & left without ttt in young age $\Rightarrow$ permanent mental affection.



IV. ↓↓ Muscle / Fat ratio

1. The muscles are markedly atrophied this atrophy is best palpated on the biceps, triceps, deltoid or quadriceps muscles.
2. At the same time S.C. fat is preserved or even increased due to adequate or high total caloric intake $\Rightarrow$ CHO facies (moon face baby).

V. Skin Manifestations

- Skin usually shows erythema & hyper-pigmentation, followed by desquamation, hypopigmentation & ulceration.
- Fissuring & cracking of the skin may give the picture of flaky paint.
- 2ry infection & even gangrene of the skin may occur. $\rightarrow$ Why?
- Napkin dermatitis is common & usually complicated by fungal & bacterial infection of the skin.
- Sites $\Rightarrow$ it can occur allover but the commonest sites are.
 1. Pressure area $\Rightarrow$ buttocks & back
 2. Flexural areas $\Rightarrow$ groin & axillae
- Causes
 1. ↓↓ Essential F.A.
 2. ↓↓ Nicotinamide & tryptophan
 3. ↓↓ Vit. A.
 4. ↓↓ Zinc

VI. Hair Changes

- The hair loses its luster, becomes easily pickable & sparse.
- The colour changes into dark brown $\Rightarrow$ light brown $\Rightarrow$ red $\Rightarrow$ yellow $\Rightarrow$ white.
- Flag sign $\Rightarrow$ the distal areas of hair are darker than the proximal areas.

Causes

1. ↓↓ Sulfer containing A.A. methionine & cystin.
2. ↓↓ Copper & Ceruloplasmin
3. ↓↓ Melanin formation.

VII. GIT Disturbance

- Anorexia & vomiting due to:
 - a. Mental changes.
 - b. Associated GIT infection.

- Diarrhea $\Rightarrow$ which may be due to
 1. 2ry Disaccharidase deficiency e.g. Lactose intolerance
 2. 2ry Infections "GE"
 3. $\downarrow\downarrow$ Digestive enzymes "Pancreatic & intestinal"
 4. Starvation diarrhea.
 5. $\downarrow\downarrow$ Fe $\Rightarrow$ atrophy of the epithelium.

VIII. Anemia

Which may be due to one of the following:

1. $\downarrow\downarrow$ Iron or Cu $\Rightarrow$ Microcytic hypochromic
2. $\downarrow\downarrow$ B₁₂ & Folic acid $\Rightarrow$ Megaloblastic.
3. $\downarrow\downarrow$ Protein $\Rightarrow$ Normocytic normochromic
4. Infection $\Rightarrow$ $\oplus$ BM or hemolysis $\Rightarrow$ Normocytic normochromic.

IX. Abdominal distention :

1. Hypokalemia (2ry to diarrhea).
2. Weak abdominal muscle.
3. Infection $\Rightarrow$ toxic ileus.
4. Malabsorption $\Rightarrow$ fermentation $\Rightarrow$ gaseous distention.
5. Giardia infection.

X. Vitamins & Minerals Deficiency

A. Vitamin A : It is very common in KWO due to :

1. $\downarrow\downarrow$ intake in diet.
2. $\downarrow\downarrow$ Storage of carotene inside the liver.
3. $\downarrow\downarrow$ Conversion carotene to vitamin A inside the liver due to Zn deficiency.
4. $\downarrow\downarrow$ Carrier proteins.

Clinical manifestations see later in vitamin deficiency.

B. Vitamin B2: Angular stomatitis, glossitis & vascularization of the cornea.

C. Vitamin D: Atrophic rickets.

D. Nicotinic acid: Pellagra.

E. Vitamin C: Scurvy.

F. Cu: Anemia, hair changes & mental changes.

G. Zn: Mental, hair & skin changes.

XI. Associated infections:

It occurs due to defective immune system (chemotaxis, intracellular killing, complement system & opsonization).

Investigations

A. Sub-Clinical Cases

1. Serum Albumin: $< 2.85 \text{ gm \%}$ but $> 2.5 \text{ gm \%}$
2. Serum Amino Acids:
 - Low serum A.A.
 - The ratio of Non-essential/ Essential
 - a. Normally = 2/1
 - b. Early cases = 2/1 – 3/1
 - c. Clinical cases = $> 3/1$

B. Clinical Cases

1. Serum proteins

- a. $\downarrow\downarrow$ Total proteins
- b. $\downarrow\downarrow$ S. Albumin $< 2.5 \text{ gm/dl}$
- c. $\downarrow\downarrow$ α , β globulins, while γ globulin may be $\uparrow\uparrow$ due to high incidence of infections.

N.B.

- Globulin is formed in the RES & severe protein deficiency is needed to cause failure of the RES.
- There is thymic atrophy $\Rightarrow \downarrow\downarrow$ T-helper cells.

2. Serum amino acids $\Rightarrow$ see before.

3. $\downarrow\downarrow$ Carrier proteins e.g. Ceruloplasmin – transferrin – Thyroid binding globulin.

4. All body enzymes are decreased except

- a. SGOT(AST) $\Rightarrow \uparrow\uparrow$ due to hepatoctytic damage & muscle damage.
- b. SGPT(ALT) $\Rightarrow \uparrow\uparrow$ due to hepatocytic damage

4. Disturbed fat metabolism:

- a. $\uparrow\uparrow$ Free fatty acids.
- b. $\downarrow\downarrow$ Serum cholesterol due to :
 - $\downarrow\downarrow$ Carrier proteins.
 - $\downarrow\downarrow$ Lipotropic factors.

5. Hypoglycemia

⇒ There's fasting hypoglycemia with impaired glucose tolerance curve.

6. CBC

⇒ Anemia of many types + ↑↑ ESR & WBCs.
⇒ "See before"

7. Urine

⇒ for UTI + ↓↓ urinary urea & hydroxy proline in urine.

8. Stools

⇒ as marasmus

8. CXR & Tuberculin test

9. Water & electrolytes:

- Na: ↑↑ total body Na but there is dilutional hyponatremia.
- K : ↓↓ due to diarrhea & hyperaldosteronism.
- ↓↓ Cu, Mg, Zn & P.
- ↓↓ Total serum Ca (↓↓ protein bound form & normal ionizable form) ⇒ no tetany.

D.D.

<i>Of edema</i>	<i>Of skin – changes</i>
1. Renal ⇒ Nephritic Nephrotic 2. Cardiac 3. Hepatic 4. Allergic ⇒ Angio-neurotic	1. Pellagra 2. Napkin dermatitis 3. Acrodermatitis enterop- Athica 4. Hartnup disease.

Napkin dermatitis

It is due to:

1. Amoniacal dermatitis: The most common cause

Mechanism ⇒ continuous soiling of the infant by his urine ⇒ bacterial splitting of urea ⇒ production of ammonia ⇒ irritation & excoriation of the skin.

2. Prolonged soiling: $\Rightarrow$ humidity $\Rightarrow$ excoriations.
3. Monilial infection: red, moist lesion with well defined raised edges. There is characteristic satellites outside the margin.
4. Over-feeding.
5. Rough closes $\Rightarrow$ continuous friction.
6. Acidic diarrhea e.g. lactose intolerance & GE.
7. Contact dermatitis: due to polysynthetic materials or application of chemicals.

Infantile pellagra

Occurs in sun exposed areas & over bony prominences.

Hartnup disease

Autosomal recessive disease characterized by defective intestinal transport of tryptophan $\Rightarrow$ Niacin deficiency $\Rightarrow$ pellagra like skin manifestations.

Acrodermatitis enteropathica

Autosomal recessive disease characterized by defective intestinal absorption of Zn.

C/P:

1. Chronic diarrhea.
2. Skin lesion as in KWO especially in perianal area.
3. Nail dystrophy.
4. Stomatitis.
5. Growth retardation.
6. Intercurrent infection.

Complications

1. Inter-current infections

2. G.E. $\Rightarrow$ dehydration & electrolyte imbalance

3. Hypoglycemia $\Rightarrow$ Why?

- $\downarrow\downarrow$ Glycogen stores inside the liver.
- $\downarrow\downarrow$ Counter-regulatory hormones of insulin e.g. catecholamines & glucagon.

4. Hypothermia $\Rightarrow$ Why?

- Severe dehydration & shock.
- Septicemic Shock.
- Impaired shivering due to muscle wasting.
- Hypoglycemic attacks.

5. DIC (bad prognostic sign) $\Rightarrow$ Why?

6. Metabolic complications:

- $\downarrow\downarrow$ Ca, Mg, Na, K.

7. HF $\Rightarrow$ Why?

- Degenerative changes in cardiac muscles.
- Anemic HF.
- Toxic myocarditis.
- Volume overload.

Marasmic – KWO

- Baby with all essential features of KWO + Wt < 60% of normal wt for his age.
- It is due to combination of:
 1. $\downarrow\downarrow$ Total caloric intake “under-nutrition”
 2. $\downarrow\downarrow$ protein “mal-nutrition”
- C/P:
 - Loss of SC fat.
 - Lack of moon face of KWO.
 - With or without skin & hair changes .
- !!! is more difficult & prognosis is bad

Pre-KWO “ CHO- baby

- Baby with incomplete picture of KWO “ Absence of one or more of the essential features”
- There is decrease body weight.
- Mental changes.
- Hair & may be skin changes.
- No edema.

Nutritional Dwarfism

In this condition, early mild to moderate protein-energy undernutrition occurs, to which adapts himself by slow growth $\Rightarrow \downarrow \downarrow$ both Wt & height " $< 10^{\text{th}}$ percentile for age" $\Rightarrow$ Proportionate dwarfism.

So, in this condition:

1. Wt for age $\Rightarrow$ low " $< 10^{\text{th}}$ percentile"
2. Height for age $\Rightarrow$ Low " $< 10^{\text{th}}$ percentile"
3. Wt for height $\Rightarrow$ normal proportionate

Causes of Hypoproteinemia

1. $\downarrow \downarrow \downarrow$ Intake
2. Indigestion & Malabsorption
 - a. Chronic diarrhea
 - b. Celiac disease
 - c. Intestinal parasites
3. $\downarrow \downarrow \downarrow$ Loss
 - a. Urinary $\Rightarrow$ Nephrotic syndrome
 - b. Intestinal $\Rightarrow$ Protein losing enteropathy.
 - c. Cutaneous $\Rightarrow$ Burns, Ulcers, Eczema.
 - d. Others $\Rightarrow$ Repeated taps for ascitis, hydrothorax.
4. Decreased Production of serum proteins "Albumin"
 - a. Liver diseases.
 - b. Inborn errors of albumin.
 - e.g. Aalbuminemia.

Management of Nutritional Diseases

1. Proper history
2. Proper Clinical examination
3. Investigations.
4. D.D.
5. Treatment.



Just do your best

Treatment of Marasmus & KWO

A. Prevention

1. Proper diet
2. Proper breast feeding.
3. Proper weaning
4. Proper vaccination esp. against measles, whooping cough, T.B.
5. Family planning.
6. Follow up of the growth of the baby by " growth curves $\Rightarrow$ for early detection & ttt.

B. Dietetic Management

1. Education of the mother about the nutritive needs of her baby & how to prepare adequate diet is essential.
2. Caloric intake / Day.
 - a. In marasmus $\Rightarrow$ 150 Cal./Kg/D
 - b. In KWO $\Rightarrow$ 120 Cal./kg/D

In 1st degree marasmus it is calculated according to the expected weight, while in 2nd & 3rd degree marasmus & in KWO it is calculated on the average weight (mid-way between expected & actual body weight).

3. The diet should supply high protein "4 gm /Kg/D" of high biological value esp. in KWO.
4. Route of administration:
 - a. Oral : By bottle, cup & spoon or dropper.
 - b. Nasogastric tube: If there's vomiting, anorexia, severe stomatitis or cleft lip & palate.
 - c. Total parenteral nutrition: if there is contraindication of oral feeding or persistent vomiting inspite of nasogastric feeding..

* ***In weaned babies*** $\Rightarrow$ Yogurt, Vegetable soup, cereals, minced meat. Then give well balanced diet..

** ***In non weaned babies*** $\Rightarrow$

1. In uncomplicated cases:

Humanized milk + protein added

N.B.

2. In lactose intolerance:

Lactose free milk + protein

3. Fat intolerance

Skimmed milk + medium chain triglyceride + protein.

- The protein added to the formula should be of high biological value.
- The amount & concentration of the formula should be increased gradually according to the tolerance of the baby, till the expected weight is reached.

C. Non-Dietetic Management

I. Emergency Management

In complicated cases the following should be done on emergency basis:

1. Shock

⇒ Stimulants & blood transfusion.

2. Dehydration

⇒ Rehydration & correction of electrolyte imbalance.

3. Hypothermia

⇒ Proper warming of the baby

4. Hypoglycemia

⇒ Glucose 10% by IV drip.

II. Blood transfusion + I.V. alimentation

1. Fresh blood ⇒ 20ml / Kg (the best)

2. FFP ⇒ 10ml/kg

3. Salt free albumin "Human" ⇒ 10ml/kg.

4. Amino-acid mixture preparation " Trophysan – Totamine - Vamine": 20 ml / Kg. ⇒ May cause hypoglycemia as they are rich in arginine a.a. ⇒ stimulation of insulin release.

It is contraindicated in HF, renal failure & hepatic failure.

N.B.

The advantages of blood transfusion are :

1. Correction of anemia.
2. ↑↑ Resistance to infection.
3. ↓↓ Edema in KWO.
4. Improvement of appetite.
5. Plasma proteins can be used for formation of the important critical proteins of the body e.g. enzymes hormones etc.
6. Correction of bleeding tendency fresh blood.

III. Antibiotics

In marasmus & KWO infections are common, either manifest or hidden.

⇒ Procaine penicillin or crystallin penicillin.

In Manifest infections ⇒ Culture & sensitivity should determine the appropriate antibiotic.

If there is moniliasis:

- Oral moniliasis ⇒ Mycostatin drops & gentian violet paint.
- Oral moniliasis ⇒ Nystatin cream & gentian violet paint.

↳ ~~Oral~~ ^{kin}

IV. Vitamins & Minerals

These should be supplied orally from the start. If diarrhea is present, we give them by IMI.

- Vit. A in high doses (50.000 IU / D) is particularly important if there is eye affection to prevent further damage & blindness.
- Zinc & magnesium should be supplemented especially in KWO.
- Oral Ca, or IV in tetany.

V. Anabolic Hormones

As Durabolin, Verabolin 1mg/Kg/D in order to help a positive nitrogen balance. However, their role in t t t is questioned.

VI. t t t of the cause

This is an essential part in management.

Q: What are the phenomena occurring during t t t of KWO ?

1. Over-Hydration during rehydration.
2. Hypokalemia ⇒ usually present at the start. Failure of diagnosis lead to death.
3. Nutritional recovery syndrome:

Which is noticed in nutritionally deficient babies, who are treated by high protein diets as in case of KWO.

It is caused by hepatic dysfunction in cases of KWO + high protein diet.

It presents by

- a. Hepatomegaly
- b. Hyper-ammonemia
- c. Encephalopathy with or without convulsions.

Usually, there are changes in the mood, behavior & level of consciousness in severe cases.

- d. Mild jaundice may be present.

Prognosis of KWO

1. Early : depends on :

- a. Age: young age $\Rightarrow$ bad prognosis.
- b. Cause : irreversible cause $\Rightarrow$ bad prognosis .
- c. Presence of complication $\Rightarrow$ bad prognosis.
- D. ttt : early ttt $\Rightarrow$ good prognosis

2. Later :

- a. Growth $\Rightarrow$ early sufficient ttt $\Rightarrow$ normal growth.
- b. Mentality $\Rightarrow$ MR occurs in early cases before 6ms or in sever cases.
- c. Liver cirrhosis $\Rightarrow$ does not occur.



Calcium Metabolism

Factors Affecting Absorption

1. PH of Duedenum

An acidic PH of the duodenum $\Rightarrow \uparrow\uparrow\uparrow$ Absorption.

Alkaline PH $\Rightarrow \downarrow\downarrow\downarrow$ Absorption.

2. Phosphate in Diet

If $\uparrow\uparrow\uparrow \Rightarrow$ precipitation of $\text{Ca}^{++} \Rightarrow \downarrow\downarrow\downarrow$ absorption.

N.B.

The Ca: P ratio in diet must be 2 : 1 or 1 : 1 for optimum absorption.

“ This is the ratio present in human milk ”

3. Other constituents of diet

A. Phytate “ in cereal grains ” $\Rightarrow \downarrow\downarrow\downarrow$ absorption

B. Oxalates “ e.g. in spinach ” $\Rightarrow \downarrow\downarrow$ absorption

C. High protein & vitamin C in diet $\Rightarrow \uparrow\uparrow$ absorption.

4. Hormonal factors

A. Vitamin D $\Rightarrow \uparrow\uparrow\uparrow$ absorption

B. Parathyroid hormone $\Rightarrow \oplus$ Formation of active form of vit - D
 $\Rightarrow \uparrow\uparrow$ absorption.

Blood Forms

- The normal plasma level is 9-11 mg%
- It is present mainly in 2 main forms:

A. Ionized form

$\Rightarrow$ The physiological active form

B. Bound form

$\Rightarrow$ Inactive form which is bound to plasma proteins

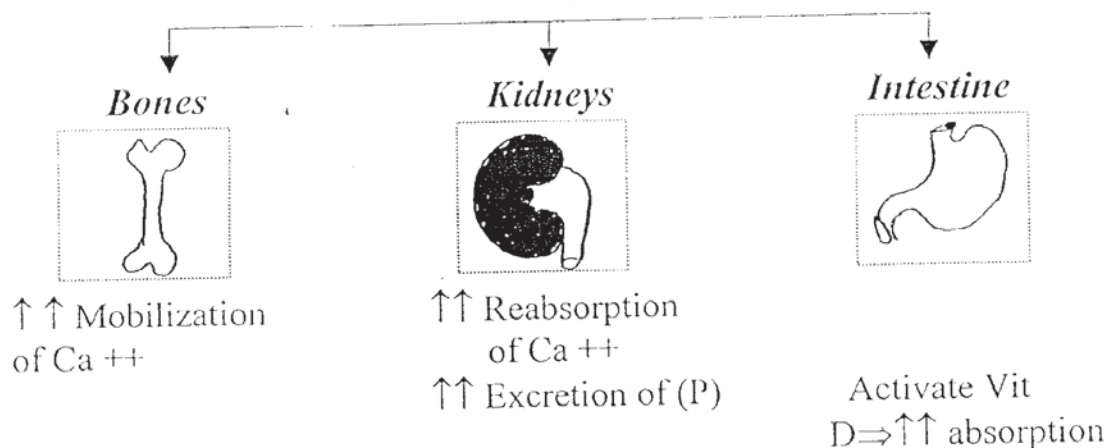
Concentraaaaaate ..

Factors Affecting Blood Ca^{++}

A. Para-thyroid hormone "PTH"

$\Rightarrow \uparrow \uparrow \uparrow \text{Ca}^{++}$
 $\downarrow \downarrow \downarrow (\text{P})$

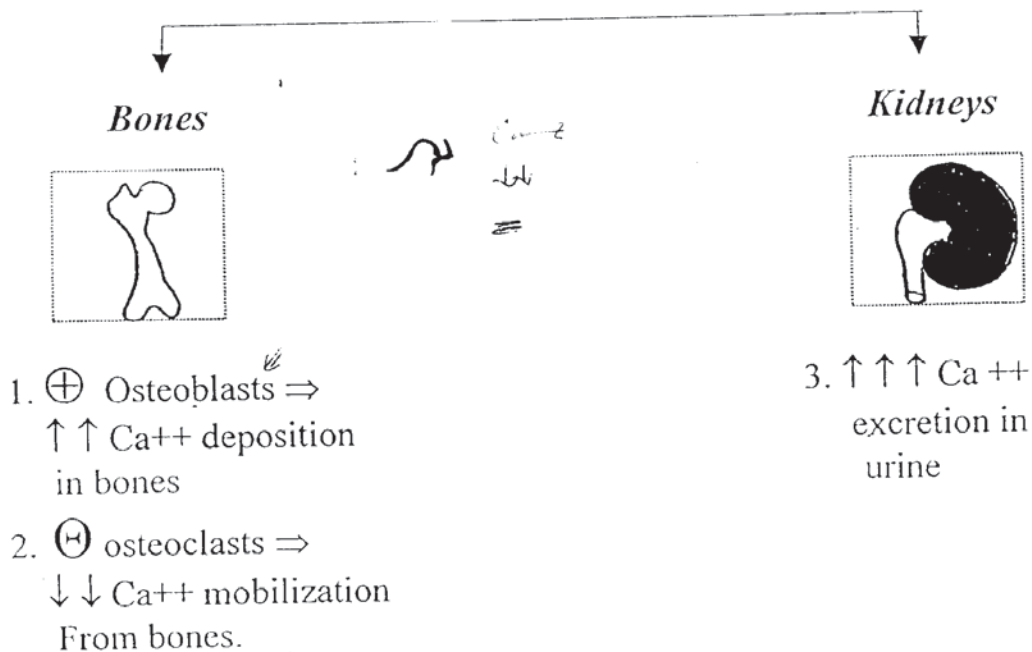
Through the following mechanisms



B. Calcitonin

$\Rightarrow \downarrow \downarrow \downarrow \text{Ca}^{++}$

Through the following mechanisms



Success wants more efforts

C. Vit - D

Bones



Deposition of Ca^{++} & P

Kidneys



Reabsorption of P & Ca^{2+}

Intestine



Absorption of Ca^{++} & P

D. PH of the blood

Acidosis $\Rightarrow \uparrow \uparrow$ Ionizable form

Alkalosis $\Rightarrow \downarrow \downarrow$ Ionizable form



Do you want to be one of
the fronts

Rickets

Definition

It is a systemic metabolic disease characterized by defective mineralization of bone & cartilage in the growing baby, leading to excessive formation of osteoid tissue, which gives way under pressure leading to deformities.

Classification

A. Vit-D Deficiency Rickets

1. Dietary deficiency of vit-D
2. Lack of exposure to UVR
3. Atrophic rickets.

B. Vit-D Resistant Rickets

I. Renal Rickets:

1. Glomerular $\Rightarrow$ Renal osteodystrophy
2. Tubular $\Rightarrow$ Iry hypophosphatemic
Rickets Lignac syndrome
De Toni-Fanconi Syndrome
Lowe's syndrome
Infantile renal tubular acidosis.
3. Vit-D Dependent Rickets
Typ I
Type II

II. Hepatic Rickets

1. Defective 25-hydroxylation
2. Toxic hepatic hydroxylation.
3. Malabsorption of Vit-D due to bile deficiency.

III. Celiac Rickets

IV. Hypo-phosphatasia

V. Hyper-parathyroidism

*Hey .. It's your way to
reach your aims*

Recent Classification

Type I: 1ry calcium deficiency “ Deficiency of $1,25 - (OH)_2 - D_3$ ”

1. Nutritional deficiency.
2. Malabsorption of Vit-D
3. Hepatic disease
4. Toxic hydroxylation.
5. Renal Osteodystrophy
6. Vit-D dependent rickets type I

TYPE II: 1ry Phosphate Deficiency : “No 2ry hyper-parathyroidism

1. 1ry hypo-phosphatemic rickets.
2. De Toni-Fanconi syndrome
3. Lignac syndrome
4. Lowe’s syndrome
5. Proximal renal tubular acidosis.
6. Phosphate deficiency or malabsorption.

TYPE III: End-Organ Resistance to $1,25 (OH)_2 - D_3$:

Vit-D – dependant rickets type II

TYPE IV: Related Conditions Resembling Rickets

- 1) Hypo-Phosphatasia
- 2) Hyper-Parathyroidism.

Vitamin – D

- It is a steroid, fat soluble vitamin.

Sources

1. Breast & Cow milk

⇒ both are deficient sources .

2. Rich sources are :

⇒ Cod liver oil, egg yolk (3-10 ug / gm)(1 ug = 40 IU),
fortified milks .

Requirements

The daily requirements are

- 400 – 800 IU/D for normal children.
- 800-1200 IU/D for PT & IUGR

Storage

⇒ Liver

Forms

1. Vit -D2 "Ergocalciferol"

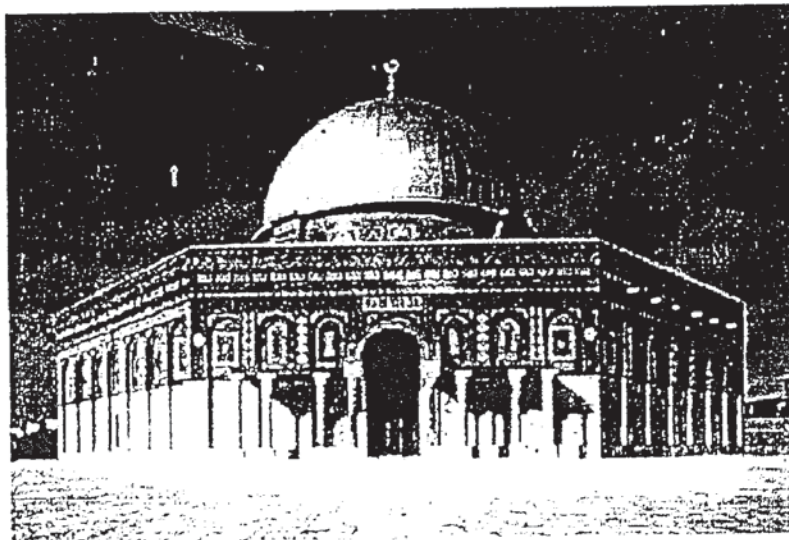
⇒ Produced by irradiation of plant "Ergosterol"

2. Vit-D3 "Cholecalciferol"

⇒ Produced by irradiation of 7-dehydro-cholesterol present in skin by UVR in the sun light(300–310 nm). These rays do not pass through ordinary window glass.

Metabolism

1. Absorption ⇒ from the small intestine along with fat in the presence of bile salts.
2. Both the absorbed Vit -D & that which is formed in the skin under the effect of UVR are carried on α 2 globulin to the liver.
3. In the liver it is hydroxylated to 25 (OH) cholecalciferol. Then carried to the kidneys to be hydroxylated at position " 1" producing 1,25 dihydroxy cholecalciferol which is the active form of vit-D. If Ca & P is high, hydroxylation in 24 position to form less active form 24,25 (OH)₂-Vit-D3.



Come on .. Do your best

Vit - D Deficiency Rickets

Etiology

1. ↓ ↓ Intake (rickitogenic diet containing)

- a. Cow milk. ✓
- b. Delayed weaning. ✓
- c. low amounts of vit D & calcium. ✓
- d. High phytate or oxalate. ✓
- e. Bad Ca/P ratio. ✓
- f. Increased alkalinity (e.g. excess beverages) ✓
- g. ↓ Vit - C ✓

2. Insufficient exposure to sun ray "UVR"

- a. Glass windows & high buildings.
- b. Cloudy & foggy weather.
- c. Heavy pollution.
- d. Overlapped infant.
- e. Dark skin infant.

3. Malabsorption of Vit-D:

- a. Malabsorption syndrome.
- b. Obstructive jaundice

4. Deficiency of the active form:

- a. Vit-D dependent rickets type 1
- b. Liver disease
- c. Toxic hepatic hydroxylation.

Contributing Factors

- 2. *Age*: 6 m – 2 years "due to rapid rate of growth"
- 3. *Rate of growth*: usually affecting preterm, & twins, but not those with slow arrested growth as crinism & marasmic patients.
- 4. *Race*: more common in dark races → Why?
- 5. *Season*: more in winter than in summer → Why?
- 6. *Atmosphere*: more common in big cities → Why?

Endochondral ossification

Normally, bone growth occurs by 2 types of ossification

1. Endochondral ossification

⇒ occurs in the epiphysis, leading to increased length of bone.

2. Subperiosteal ossification.

⇒ ↑ ↑ bone thickness.

In the normal epiphysis, the following layers are present & can be visualized microscopically:

a. Zone of resting cartilage

Composed of a single layer of non dividing resting cartilage cell

b. Zone of proliferating Cartilage "ZPC"

- Composed of 4-6 layers of dividing chondroblasts, regular in arrangement.
- It is not vascular & no calcium is deposited.

c. Zone of provisional calcification.

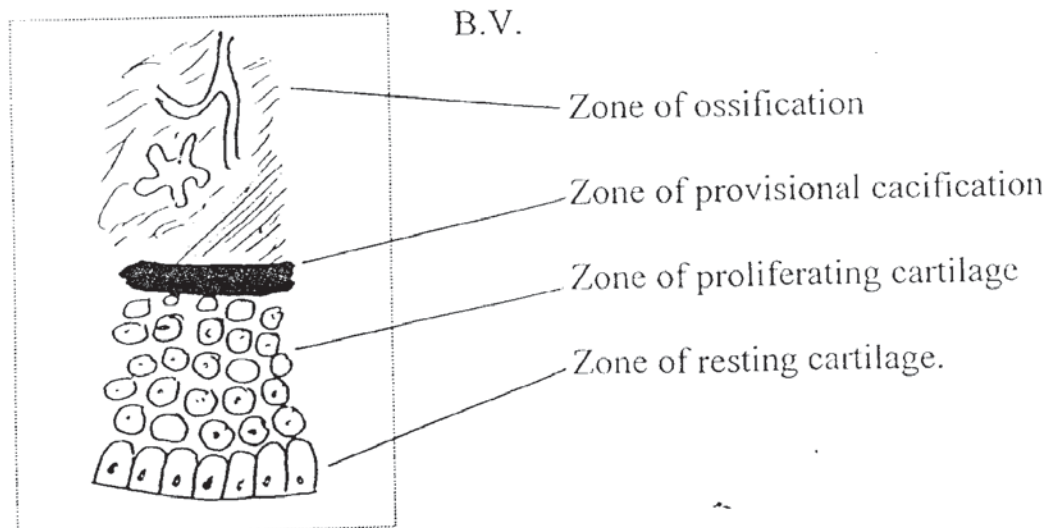
- The chondroblasts becomes swollen & vacuolated.
- The enzyme alkaline phosphatase splits PO_4 group from organic phosphate compounds in the local alkaline medium.
- This facilitate deposition of Ca^{++} phosphate salts in the matrix forming the epiphyseal line.

⇒ This line appears as sharp dense line at the end of metaphysis in X-ray.

d. Zone of ossification

- The degenerating cartilage cells are invaded by capillaries & connective tissue including osteoblasts, derived from B.M.
- The osteoblasts deposit a layer of osteoid which becomes rapidly mineralized.

So the cartilage is ultimately replaced by bone.



Pathology

In Active Rickets

- ✓ 1. There is failure of the cartilage to complete its cycle of proliferation & degeneration.
- ✓ 2. There's failure to deposit Ca^{++} salts $\Rightarrow$ excessive proliferation of cartilage.
- ✓ 3. This proliferating cartilage without calcification at the line of provisional calcification $\Rightarrow$ *Fraying* of this line in X-ray.
- ✓ 4. Failure of deposition of Ca^{++} salts at ZPC $\Rightarrow$ deposition of an uncalcified osteoid tissue.
- ✓ 5. When this tissue becomes compressed by pressure $\Rightarrow$ *Cupping & broadening* of the metaphysis occurs.
6. Calcium salts are resorbed from the pre-existing cortical bones due to physiological hyper-parathyroidism $\Rightarrow$ *Rarefaction* of bones in X-ray.
7. Sub-peri-osteal deposition of unmineralized osteoid tissue $\Rightarrow$ *Double periosteal lines* in X-ray.
8. The shaft loses its rigidity $\Rightarrow$ *deformity & fracture*.
9. The fractures are characteristically of *green-stick* type, which means that only one cortex of the bone is fractured while the other is intact.

In Healing Rickets

1. Calcification takes place in the ZPC. $\Rightarrow$ well demarcated line in X-ray film.
2. Its calcification is not continuous with the shaft i.e. uncalcified osteoid tissue between them.

In Healed rickets

1. The osteoid tissue between ZPC & the shaft becomes mineralized.
2. Through the process of bone remodeling the bone deformities are gradually corrected.
3. If deformities are severe $\Rightarrow$ Spontaneous correction may be impossible & surgery may be indicated.

C/P

C/O

1. Delayed motor milestones e.g. sitting, standing, crawling, walking....etc.
2. Delayed dentition.
3. Deformities of the bones.
4. One of the complications.

History:

History of

1. Inadequate Vit-D intake.
2. Lack of exposure to sun.
3. Cow milk feeding.
4. Anti-convulsant drugs.
5. Delayed weaning.
6. No supplementation of diet with Vit-D
7. Symptoms of complications.



Work hard

..

concentrate

O/E

A. Bony Manifestations

1. Skull

b. Craniotables

Which disappears at the age of 1 year even if untreated.

d. Delayed eruption of teeth.

3. Spine

a. Kyphosis.

b. Scoliosis.

c. Kypho-scoliosis.

4. Limbs

a. Broadening of the lower radio-ulnar epiphysis.

b. Marfan Sign ⇒ horizontal groove on both malleoli ⇒ due to hypertrophy of the epiphysis at two different sites.

c. Déformities.

Genu varum

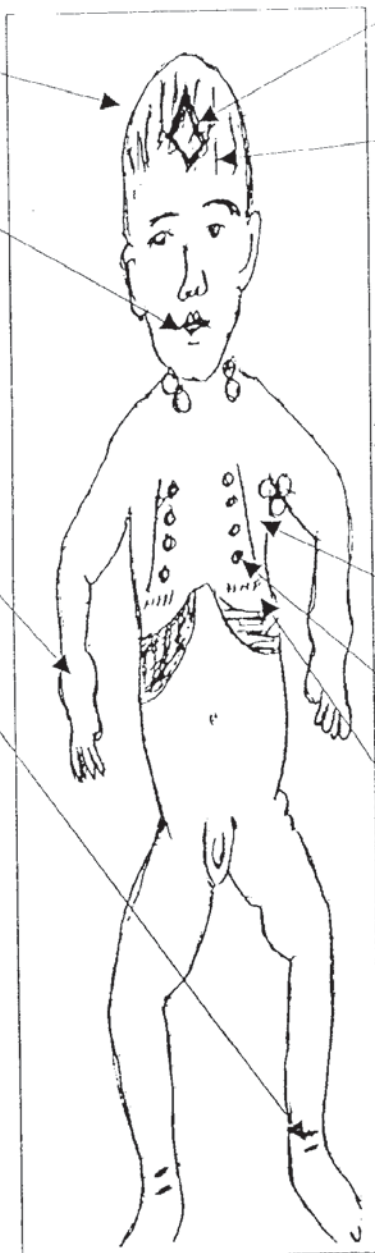
Genu valgum

Genu recurvatum.

Coxa Vara

Bowing of the forearm

Contracted pelvis..



a. Delayed closure of A.F.
"Anterior fontanell"

c. Frontal & parietal bossing ⇒ due to deposition of osteoid tissue at the center of ossification of these bones.

2. Chest

a. Pigeon Chest ⇒ The sternum is pushed forwards leaving a longitudinal groove on each sides.

b. Rickety rosary ⇒ thickening & broadening of the costo-chondral junction.

c. Harrison sulcus ⇒ horizontal groove at the lower part of the chest at the level of insertion of the diaphragm

5. Ligaments & Muscles

Laxity of ligaments, Hypotonia & Weakness of muscles ⇒

Kypho-scoliosis

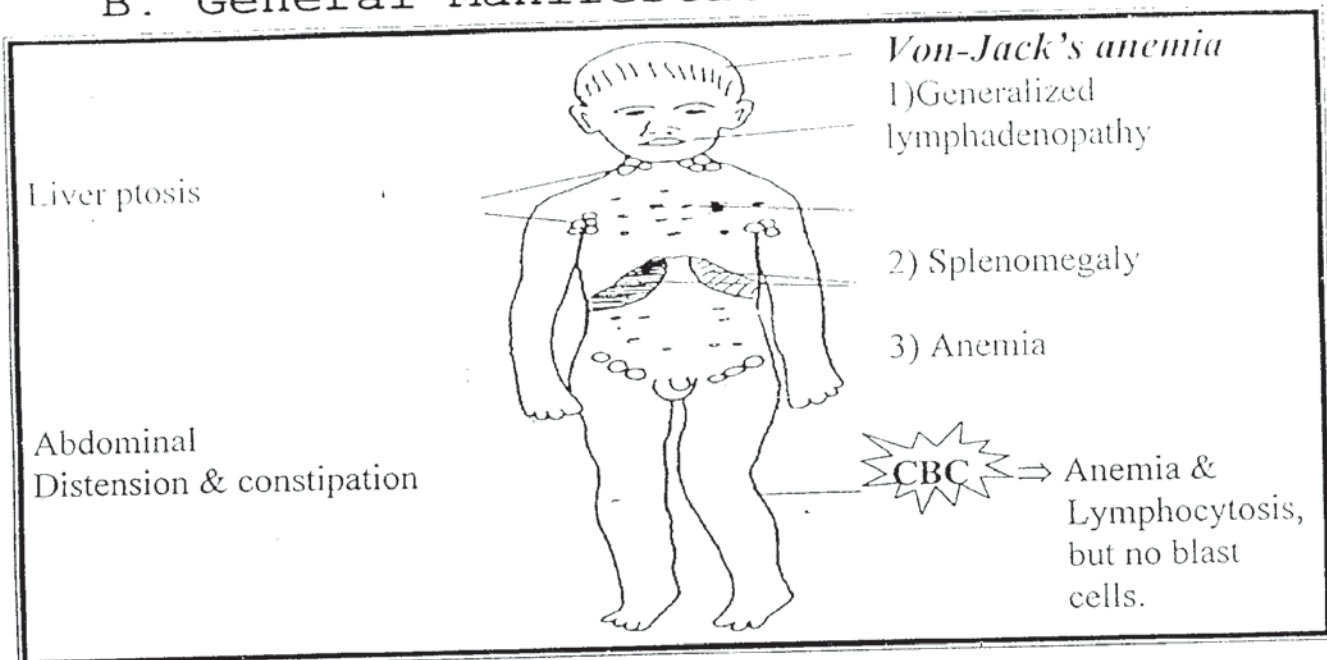
Pott belly abdomen

viscero-ptosis

Umbilical hernia.

It is due to hypo-phosphatemia.

B. General Manifestations.



Complications

1. Respiratory $\Rightarrow$ Pneumonia
Bronchopneumonia
Bronchitis
2. GIT $\Rightarrow$ Constipation due to hypotonia & GE.
3. Bone Fractures & deformities $\Rightarrow$ dwarfism
4. Anemia "Von Jack's anemia"
5. Tetany
6. Obstructed labor "later"
7. Dental caries

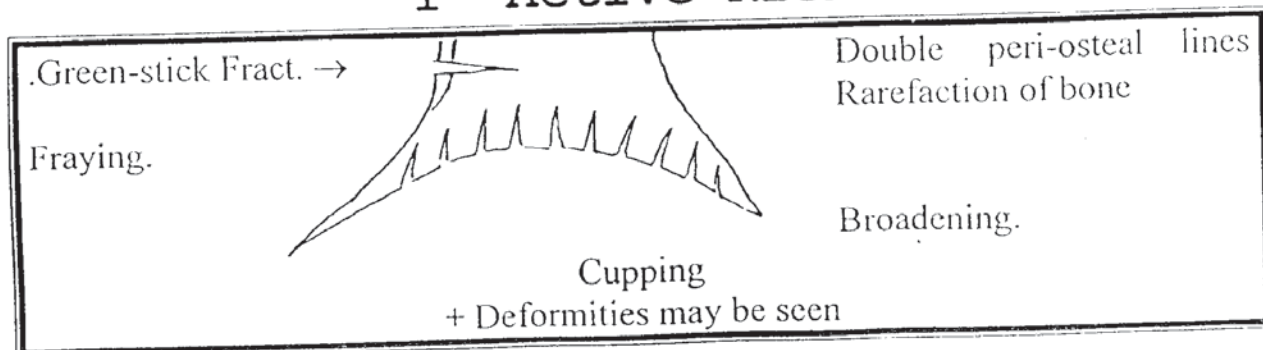
Q: What are the causes of tetany in Rickets?

1. Severe cases of rickets.
2. Failure of the parathyroid gland
3. Shock therapy with vit-D without calcium supplementation.
4. Bone stores of Ca^{++} are exhausted.

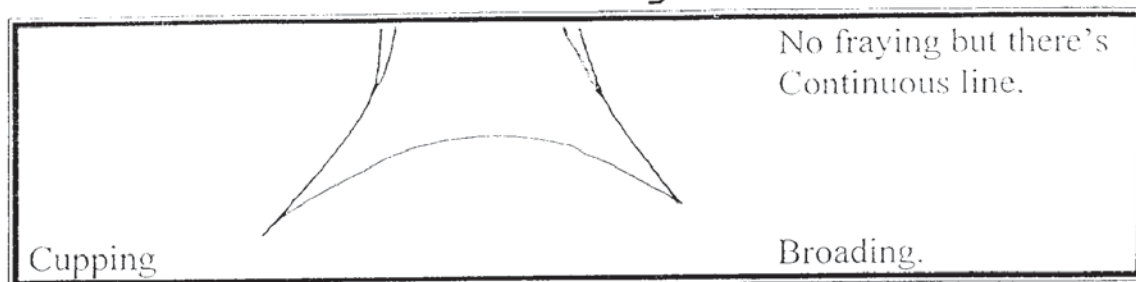
Investigations

A. X-ray of bones

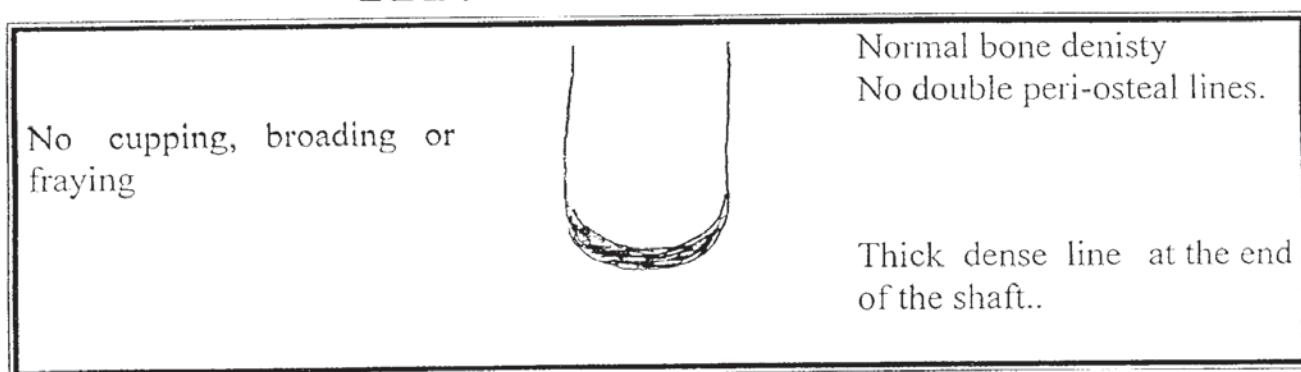
I- Active Rickets



II. Healing Rickets



III. Healed Rickets



B. Biochemical Changes

1. Serum Ca^{++} "N: 9-11 mg/dl"

⇒ Low normal

It may be reduced to tetanic level → Why?

N.B.

It is initially $\downarrow\downarrow \Rightarrow \uparrow\uparrow$ parathyroid hormone mobilization of Ca^{++} From bones to the blood maintaining normal calcium level $\uparrow\uparrow$ Loss of (P) in urine → $\downarrow$ (P).

2. Serum Po_4 "N: 4.5 – 6.5 mg/dl"

→ Reduced 1.5-3 mg / dl

Ca X P (Howland formula) is low < 30 (N > 40).

3. Serum Alkaline phosphatase

→ Elevated > 500 IU / L "N: 145-200 IU / L" due to $\uparrow\uparrow$ Osteoblastic activity. It is 1st laboratory parameter to change in rickets & last to return to normal after complete healing.

Others

5. Parathyroid hormone level & urinary c-AMP ⇒ $\uparrow\uparrow\uparrow$.

6. Serum 25 (OH) D3 $\downarrow\downarrow$ (N: 20-80 ng / ml, being higher in summer) & serum 1,25 (OH)2D3 is $\downarrow\downarrow$ (N: 25-45 pg / ml).

7. Generalized amino-aciduria: as vitamin D is essential for normal function of renal tubules.

8. Urine Ca $\Rightarrow$ Absent.

9. Urine PO₄ $\Rightarrow \uparrow \uparrow \uparrow$

D.D.

I. From other causes of inability to walk.

II. From other causes of craniotables:

1. Hydrocephalus.
2. Premature.
3. Congenital syphilis.
4. Osteogenesis imperfecta.
5. Some normal newborn near sutures.

III. Rickety rosary:

1. Hydrocephalus.
2. Critinism.

IV. Delayed closure of A.F.

1. Hydrocephalus
2. Critinism
3. Mongolism.
4. Osteogenesis imperfecta.

V. Delayed teething.

1. Critinism.
2. Mongolism.
3. Osteogenesis imperfecta.

VI. Spine deformity.

$\Rightarrow$ Pott's disease.

Other causes of short stature.

t t t

A. Prevention

1. Exposure to UVR
2. Supplementation of the diet with the daily requirements of vit. D, 400-800 IU day.
3. Premature babies should receive 800-1200 IU/D as early as 2nd -4th month of life.

B. Active t t t

1. Vit-D:

2000-6000 IU/D for 2 months or shock therapy as 600.000 IU by deep IMI/2 weeks for 3 doses.

2. Oral calcium intake together with vit-D

After complete healing $\Rightarrow$ Vit. D should be given in a dose
400- 800 IU/D

3. Surgical correction of deformities after complete healing.

4. t t t of complications.

Renal Rickets

Glomerular Ricket or Renal Osteodystrophy

Bone disease is one of the main features of chronic glomerular insufficiency & chronic renal failure.

Etiology

The most common causes are:

1. Chronic glomerulonephritis.
2. Chronic pyelonephritis.
3. Polycystic kidneys.
4. Chronic renal failure of any other causes.

Pathogenesis:

1. Renal parenchymal damage $\Rightarrow$ failure of renal hydroxylation of vit-D
2. $\downarrow\downarrow\downarrow$ GFR $\Rightarrow$ (P) retention $\Rightarrow \uparrow\uparrow$ (P)
 H^+ retention $\Rightarrow$ Acidosis.
 - a. $\uparrow\uparrow(P) \Rightarrow \oplus$ Parathyroid gland $\Rightarrow \uparrow\uparrow$ PTH $\Rightarrow$ bone resorption & picture of osteitis fibrosa cystica.
 - b. Acidosis $\Rightarrow \uparrow\uparrow$ solubilization of bone Ca^{++} salts.

C/P

1. Manifestations of CRF

- a. Marked growth failure & dwarfism due to
 - Under-nutrition.
 - Osteodystrophy
 - Hormonal abnormalities.
 - Medications esp. steroids.
- b. Anemia.
Due to
 1. $\downarrow\downarrow$ Erythropoietic factor
 2. Uremia $\Rightarrow \ominus$ BM
- c. Hypertension

2. Rickets

- ⇒ Bone deformities
- Pathological fracture.
- Dental abnormalities.

Investigations

A. Bone X-ray

- ⇒ Picture of rickets "active"
- Marked osteopenia & cystic like changes "Osteitis Fibrosa"
- Cystica → Why?

B. Biochemical

1. Ca++ ⇒ Normal or low
"No tetany due to acidosis"
2. (P) ⇒ ↑↑ "The only type of rickets in which (P) is high"
3. Alkaline phosphatase ⇒ ↑↑↑
4. Renal function tests ⇒ Impaired
⇒ ↑↑ Urea
↑↑ Creatinine.

C. CBC ⇒ Normocytic normochromic anemia.

t t t

1. t t t of the original renal condition

2. If there's Renal Failure

- a. Dialysis.
- b. Renal transplantation.
- c. Erythropoietin ⇒ for correction of anemia.
- d. NaHCO_3 ⇒ For correction of acidosis.

3. Rickets

- a. Restriction of (P) in diet & Oral administration of Aluminum hydroxide, Aluminum Carbonate ⇒ bind to (P) in intestinal lumen ⇒ ↓↓ absorption.
- b. ↑↑↑ Ca++ intake
- c. Active vit-D administration ⇒
e.g. Dihydroxycholesterol "AT 10"
20 Ug/Kg/d
or Calcitriol "1,25 (OH)₂ - D₃"
20-50 ng/Kg/d
- d. Surgical correction of deformities
- e. Parathyroidectomy ⇒ if there's 2ry hyper-parathyroidism refractory to t t t.

Tubular Rickets

Primar hypophosphatemic rickets (XL-D)

⇒ Both males & females are affected, but the clinical picture is more sever in males.

Pathogenesis

2 Pathogenic mechanisms ⇒ Rickets

1. ↓↓ Tubular reabsorption of (P) ⇒ (P) loss in urine "phosphaturia"
⇒ ↓↓ (P)
In the blood "Hypo-phosphatemia":
2. Defective renal hydroxylation of vit-D at position 1

C/P

1. The general condition of the patient is good.
2. Waddling gait.
3. Short stature.
4. Teeth abnormalities.
5. Bowing of lower limbs, genu varum, genu valgum, coxa vara.
6. No tetany, rickety rosary or harrison sulcus.

Investigations

1. Serum Ca^{++} ⇒ Normal or slightly ↓↓
2. Serum (P) ⇒ Markedly ↓↓↓
3. Alkaline phosphatase ⇒ ↑↑↑
4. No evidence of hyper-parathyroidism i.e. No cystic changes in the bones.

ttt

1. ↑↑↑ (P) intake:
Young children ⇒ 0.5 - 1 gm/day.
Older children ⇒ 1-4 gm/day
In the form of Na or K phosphate
2. Active Vit-D ⇒ as in Renal osteodystrophy.

De Toni Fanconi Syndrome

There's multiple defects of the proximal renal tubules to reabsorb the following:

1. (P) $\Rightarrow$ Phosphaturia + Hypophosphatemia
2. Glucose $\Rightarrow$ glucosuria.
3. A.A. $\Rightarrow$ generalized amino-aciduria. In addition, there may be:
4. K⁺ $\Rightarrow$ Hypokalemia + Hyperkaluria.
5. HCO₃ $\Rightarrow$ Bicarbonaturia + metabolic acidosis.

Etiology:

1. Idiopathic : is the most common:
It may be sporadic, AR or AD.
2. 2ry to: Renal toxin as mercury, lead, cadmium or exposure to outdated tetracyclines.
3. In association with certain inborn errors of galactosemia-Tyrosinemia- Lowe syndrome-Wilson disease.

C/P

1. Dwarfism + Failure to thrive.
2. Rickets $\Rightarrow$ due to
 - a. Hypophosphatemia.
 - b. Acidosis.

It doesn't respond to ordinary doses of Vit -D

3. The general condition is usually bad due to $\Rightarrow$ Acidosis.
 $\Rightarrow$ Hypokalemia.
4. Vomiting, Polyuria, Polydipsia & Constriction.
5. Weakness, fever with dehydration & metabolic acidosis.

Investigations

1. $\downarrow\downarrow$ K⁺
2. $\downarrow\downarrow$ P
3. Glycosuria.
4. Generalized aminoaciduria.

ttt

1. ttt of the cause in 2ry type.
2. Active vit.D : as renal osteodystrophy.
3. $\uparrow\uparrow\uparrow$ (P) intake : as before.

4. Adequate calcium intake.
5. $\uparrow\uparrow\uparrow$ (K) intake : KCL 2-3 mEq/Kg/D.
6. NaHCO₃ :For correction of acidosis.

Lignac syndrome (AR)

There is accumulation of cystine in various tissues (spleen , liver , BM, LN ,kidney ,cornea & conjunctiva)

C/P

As Fanconi \$ in addition to :

1. Photophobia due to corneal affection.
2. HSM.
3. Renal failure may occur.

Investigations:

1. Slit lamp examination of cornea.
 $\Rightarrow$ refractile cystine crystals.
2. Lab. Findings of fanconi syndrome.

ttt

As fanconi syndrome +

1. D-Penicillamine $\Rightarrow$ for chelation of cystine.
2. Recently: Cysteamine $\Rightarrow$ binds to SH-group of cystine.
3. If RF $\Rightarrow$ Dialysis or renal transplantation.

Infanitle Renal Tubular Acidosis: Lightwood \$ "AR"

RTA is classified into

Proximal RTA (type II) : $\Rightarrow$ Resulting from reduced proximal tubular reabsorption of HCO₃.

Distal RTA (type I) : $\Rightarrow$ Resulting from reduced distal tubular secretion of hydrogen ion..

1. Metabolic acidosis.
2. Hypophosphatemia.
3. Hypokalemia.
4. Hyperchloremia.

ttt

1. ttt of acidosis & hypokalemia.
2. Correction of hypophosphatemia.
3. Active form of Vit-D

Lowe's "Oculo-Cerebro-Renal (XLR)

1. Ocular $\Rightarrow$ Cong cataracts-Glucoma Buphthalmos.
 2. Cerebral $\Rightarrow$ MR- severe hypotonia & hypo-reflexia.
 3. Renal $\Rightarrow$ Inability to acidify urine & features of fanconi syndrome.
- Rickets is due to acidosis & hypophosphatemia.

Vit.D Dependent Rickets "AR"

Type I

$\Rightarrow$ Due to hereditary defect in renal hydroxylation of Vit. D $\Rightarrow \downarrow \downarrow$
 $\text{Ca}^{++} \& \text{P} + \uparrow \uparrow \text{Alkaline phosphatase} \Rightarrow \uparrow \uparrow \text{PTH}$

ttt

Active form of Vit. D

Type II

$\Rightarrow$ Due to target organ resistance to Vit. D
There is short stature & alopecia totalis.
Rickets may respond to very high doses of Vit D "active form"



To be the first ..
You must have big harvest

Hepatic Rickets

Due to

1. Defective hydroxylation at position 25.
2. Malabsorption of Vit-D due to absence of bile salts in cases of obstructive Jaundice.
3. Toxic hepatic hydroxylation – in case of anti-convulsant therapy.

These drugs accelerate metabolism & catabolism of Vit-D.

Celiac rickets

Due to malabsorption of Vit-D "Fat soluble" $\Rightarrow$ These F.A. will bind to Ca^{++} $\Rightarrow$ Ca^{++} soaps formation $\Rightarrow$ will precipitate in the intestine $\Rightarrow$ Ca^{++} malabsorption.

Hypo-Phosphatasia AR

- Due to cong. Absence or deficiency of alkaline phosphatase $\Rightarrow$ defective mineralization of bones.
- Serum Ca^{++} is high $\Rightarrow$ Nephro-calcinosis
- Seru. ALK phosph $\Rightarrow$ Markedly low.
- Urine characteristically contains increased amount of phospho-ethanolamine.

ttt

$\Rightarrow$ infusion of plasma rich in Alkaline phosphatase.

Hyper-parathyroidism

Hyperplasia, adenoma or carcinoma of the parathyroid gland $\Rightarrow$ $\uparrow\uparrow$ PTH $\Rightarrow$ picture of osteitis fibrosa cystica. Both serum Ca^{++} & alkaline phosphatase are increased.

ttt

Adenoma $\Rightarrow$ excision

Hyperplasia $\Rightarrow$ total parathyroidectomy + post operative supplementation with Ca^{++} is essential.

Nutritional Assessment

It is important for prevention, early detection & ttt of nutritional disorders.

Methods

1. Dietary evaluation.
2. Clinical evaluation.
3. Anthropometric evaluation.
4. Laboratory findings.

I. Dietary evaluation

1. Measuring the quantity & quality of food intake regarding the major food elements, vitamins, minerals and trace elements & comparison with the individuals requirements.
2. History of any abnormality in feeding practice.
3. Collection of information about food consumption by:
 - a. Records based on 24 hrs recall
 - b. 3-7 days feeding history or,
 - c. The usual pattern of food consumption. "quantity& quality"

II. Clinical evaluation

By full clinical examination we can detect cases of severe nutritional deprivation or even mild to moderate nutritional disorders.

III. Anthropometric evaluation

It is the measurement of physical dimensions of the human body at different ages & comparison with standard references. To determine abnormalities in growth.

1. Weight "Wt"

- $\Rightarrow$ Good index for acute nutritional status.
- It is plotted on 2 graphs $\Rightarrow$ Wt. for age.
Wt for height.
- Under – weight is less than the 10th percentile.
- Over – weight is more than the 90th percentile.

2. Length ~ Ht

- $\Rightarrow$ It indicate chronic growth failure which may be due to chronic under nutrition
- If $< 10^{\text{th}}$ percentile $\Rightarrow$ Dwarfism.

3. Wt for Ht

- It is important for measuring body built & distinguishes wasting from dwarfism.

4. Growth Velocity:

- It is expressed by cm / Year & plotted on special curves.
- It is a more sensitive method for assessing growth failure or slow growth.

5. Triceps skin fold thickness.

$\Rightarrow$ An indicator for total body fat.

Because about $\frac{1}{2}$ body fat is in the S.C. layer.

It is measured at the midpoint between the acromion & olecranon at the non dominant arm during relaxation.

It is more than 13mm after 1 year age.

6. Mid-arm circumference & ms. mass.

By measuring the triceps skin fold thickness & the midarm circumference, we can calculate the ms. mass, which is a good indicator of nutritional status.

The mid-arm circumference is normally more than 13.5 cm after 1 year of age.

7. Chest / head circumference ratio

- At birth this ratio is less than 1
 - At 6 months $\Rightarrow$ "1" & gradually increases later on.
- A ratio < 1 after 6m is one of the early features of malnutrition.

IV. Laboratory Evaluation

It is used to confirm nutrient deficiencies which has been determined by dietary, clinical or anthropometric evaluation.

It can also help in diagnoses of subclinical cases e.g.
Hb %, Hct, S. albumin & other proteins ... etc.

It almost been done

Vitamins & Minerals Deficiency

Vit - B2

1. Angular stomatitis
2. Glossitis
3. Vascularization of the Cornea.

!!!

⇒ 10 mg/D oral
+ other Vit.

Nicotinamide

1. Smooth red tongue
2. 4 Ds ⇒ Dementia.
Diarrhea
Dermatitis
Death

!!!

⇒ 50-300 mg/D oral or IM
+ well balanced diet.

Vit-C

⇒ Scurvy

1. Hgic manifestations "gums"
2. Poor wound healing.
3. Sub-periosteal hge.
4. Tender limbs.
5. Susceptibility to infection

!!!

⇒ 100 -200 mg/D oral or IV
or orange juices.

Vit-A

Eyes ⇒ Night blindness
Bitot spots
Xerosis
Corneal ulceration

Skin $\Rightarrow$ Hyperkeratosis follicularis "Goose skin"

!!!

5000 U/D oral + 25.000 U/M till recovery.
Then 5000 U/D (Oral)

Vit-K

Bleeding tendency due to hypoprothrombinemia "II, VII, IX, X"

!!!

1 mg/Kg/D

Vit-E

Hemolytic anemia in premature

Vit-B1

$\Rightarrow$ Beri beri

Vit-B6

CNS $\Rightarrow$ convulsions + polyneuropathy

Anemia $\Rightarrow$ Hypochromic

Glossitis, seborrhea.

Copper

$\Rightarrow$ Anemia + hair changes

Zinc

$\Rightarrow$ Acrodermatitis enteropathica.

Vitamin Toxicity or Hypervit.

Hypervitaminosis D

Usually due to high doses > 20.000 U/D for 1-3 m.

C/P

1. GIT: Anorexia
Vomiting
Constipation
2. Kidney: Polyuria

Dehydration
Renal stones
Nephrocalcinosis.

3. Generalized weakness, hypotonia.
4. Hypercalcemia $\Rightarrow$ Hypercalcuria
Metastatic calcifications "Renal & other tissues"
Calcific aortic stenosis

Investigations

1. Serum $\text{Ca}^{2+} \Rightarrow \uparrow \uparrow \uparrow$
2. $\uparrow \uparrow \uparrow \text{Ca}^{2+}$ in urine "Hypercalcuria"
3. X-ray $\Rightarrow$ show metastatic calcification
Nephrocalcinosis
Osteoporosis.

D.D.

1. Hyperparathyroidism
2. Idiopathic hypercalcemia
3. Chronic renal failure.

ttt

A. Prevention

$\Rightarrow$ Avoid high doses of Vit.D. for long periods.
But if this is necessary, monitoring of serum Ca^{++} is important.

B. Curative

1. Stop Vit-D till symptoms disappear & serum Ca^{++} becomes normal
2. Low Ca^{2+} diet.
3. Correction of dehydration.
4. $\text{Al}(\text{OH})_3$ gel orally $\Rightarrow$ to $\downarrow \downarrow \text{Ca}^{2+}$ absorption.
5. EDTA $\Rightarrow$ to chelate Ca^{++}
6. Cortisone in severe cases
 $\Rightarrow$ Why?

Hypervitaminosis A

A. Acute

⇒ usually after ingestion of 300,000 U or more.

C/P ⇒ Nausea, vomiting + ↑ ICP ⇒
Bulging fontanel, papilledema,
⇒ Pseudo-tumor cerebri

B. Chronic

Anorexia
Tender swelling of bones.
Cranio-tables
Desquamation of palms & soles.
Fissuring of angles of mouth.

X-ray ⇒ cortical hyperostosis of bones.

Vit- K toxicity

Synthetic vit-K is an oxidizing agent

⇒ hemolysis of RBCs ⇒ Hyper-bilirubinemia & kernicterus in
The premature & G-6 – P D deficient newborn.

Infantile Tetany

It is a state of hyper-excitability of the central & peripheral nervous system resulting from abnormal ionic concentration in the fluid bathing nerve cells & peripheral nerves.

Etiology

A. Hypocalcemia

1. Vit – D deficiency or abnormalities in Vit-D metabolism.

2. Hypo-parathyroidism.

- Early neonatal hypocalcemia (1st 72 hrs) ⇒ infant of diabetic mother, preterms, IUGR, perinatal asphyxia.
- Late neonatal hypocalcemia (5-10 days) ⇒ A high phosphate food such as cow milk depresses serum Ca through the deposition of Ca in bone while the infant parathyroid is not yet able to respond by ↑↑ PTH.

- c. Aplasia or hypoplasia of parathyroid e.g. DiGeorge \$, CHARGE or VATER \$.
 - d. Surgical removal parathyroid gland.
 - e. Infiltration of parathyroid gland as in hemosiderosis or Wilson's disease.
 - f. Autoimmune destruction of parathyroid gland.
 - g. Familial.
3. Exchange transfusion.

B. Alkalosis.

1. Hyper-ventilation.
2. Alkali-therapy " NaHCO_3 "
3. Excessive loss of gastric HCL e.g. "Vomiting"



C. Hypomagnesemia.

1. Chronic diarrhea.
2. Malabsorption of Mg^{++}
3. Exchange transfusion.
4. Total parenteral nutrition without sufficient Mg.
5. Nephrotoxic medication & diuretic therapy.

C/P

A. Manifest tetany

If serum $\text{Ca}^{++} < 7 \text{ mg/dl}$

1. Carpo-pedal spasm
2. Laryngeal spasm
3. Convulsions in infants & newborn.

B. Latent Tetany.

If serum Ca^{2+} is 7-9 mg/dl

1. Chevostek sign

Tapping the facial nerve "anterior to external auditory meatus" $\Rightarrow$ contraction of orbicularis oris ms.

2. Trousseau sign

Occluding the arterial flow to the forearm by inflating a blood pressure cuff over systolic pressure for 3 min $\Rightarrow$ appearance of the typical carpo-pedal spasm.

3. Peroneal sign

Tapping the peroneal nerve over the neck of the fibula $\Rightarrow$ dorsi-flexion & eversion of the foot.

4. Prolonged QT interval.

ttt

A. Immediate

1. Ca gluconate 10 %

⇒ 2ml / Kg slowly IV

2. If no response ⇒ search for the etiology & correct the alkalosis or Mg deficiency "0.2 ml/kg IM"

B. Maintenance

1. Diet rich in Ca^{++} or Ca chloride orally.

2. Vit – D for ttt of rickets & improving Ca-absorption.



You need help..
W're here

Neonatology

The Newborn

- The neonatal period is the 1st 4 weeks of life after birth.
- Immediate or early neonatal period is the first week of life.
- The late neonatal period is the next 3 weeks of life.
- The perinatal period is the period from 20th week of gestational life through the 28th day after birth.
 - As physiological adaptation and adjustment of the baby to the extra uterine environment occur in that period, neonatal mortality accounts for 65 % of deaths in the 1st year of life and it is highest during the 1st day after birth.

Classifications

According to:

A. Gestational period:

1. Preterm less than 37 wks of gestation
2. Full term between 37 and 42 wks of gestation
3. Post term more than 42 wks of gestation.

B. Birth weight:

1. Large birth weight (macrosomia) = 4000 gm or more after birth.
2. Normal birth weight (NBW) = 2500 to 4000 gm after birth.
3. Low birth weight (LBW) = 2500 gm or less after birth.
4. Very low birth weight (VLBW) = 1500 gm or less after birth
5. Extremely low birth weight (ELBW) = 1000 gm or less after birth
6. Impossibly low birth weight (ILBW) = 750 gm or less after birth

C. Size for gestation:

1. Small for gestational age (SGA)" small for date " light for date":
Birth weight less than 10th percentile for gestational age.
2. Appropriate for gestational age (AGA):
Birth weight between 10th and 90th percentile for gestational age.
3. Large for gestational age (LGA):
Birth weight more than 90th percentile for gestational age.



Postnatal differentiation between PT & FT:

	Preterm	Full term
1. Measurements		
Weight	< 2.5 kg	3-3.5 kg
Length	< 47 cm	50 cm
Head circumference	< 33 cm	35 cm
Chest circumference	< 30 cm	33 cm
2. Vitality		
Cry	Feeble	Good
Sucking power	Weak	Good
Muscle tone	Poor	Good
Muscle movement	Slow, infrequent	Strong, frequent

Characteristics of the normal FT newborn

1. Body proportions :

- * The head : It is relatively large, the face is rounded & the mandible is relatively small.
- * The chest : It is rounded rather than flattened antero-posteriorly.
- * The abdomen : It is prominent.
- * The extremities are relatively short.
- * The mid-point of the stature is at the umbilicus (in adult at the symphysis pubis).
- * The predominant posture is partial flexion.

2. Color :

- * The normal color is rosy pink.
- * Mongolian spots : It is purplish mottling over the back & buttocks (not pathological).

3. Skin :

- * At birth the infant is covered with cheesy white material adherent to the skin called vernix caseosa.
- * The normal skin is dry , peeling is found at the ankles but extensive peeling & transverse fissuring over the abdomen denotes dysmaturity.
- * At birth lanugo hair usually covers shoulders.

- * Milia : It is distended sebaceous glands appears as white spots over nose & cheeks (needs no ttt).
- * Capillary hemangiomas are common over the eye lids , forehead & back of the neck .
- * Umbilical stump darkens in color , dries & then falls by the end of the first week.

4. Measurements :

- * The length : 50 cm.
- * The weight : 3.400 kg.
- * Head circumference : 33 cm.
- * RR : 30-40 / min.
- * Pulse : 120-160 / min .
- * BP : 70-85 / 40-60 mmHg.
- * Temperature : At delivery the infant's temperature is the same as his mother . After delivery there is a transient fall in temperature which is usually restored within 4-8 hours.

5. cardiac signs :

- * The heart sounds have the characteristic tic tac rhythm .
- * There may be transient innocent cardiac murmurs .
- * CXR : the heart seems to be large in respect to the shape of the chest so the apex is located in the 4th intercostal space outside the mid-clavicular line.

6. G.I.T. :

- * The 1st stools will be generally passed within 24 hrs which consist of meconium .
- * By establishing breast feeding , meconium stools start to be replaced by transitional stools on the 3rd or 4th day (greenish brown) , later become golden yellow.
- * Frequency : 3-5 / day by the end of the 1st week .
- * Melena in the newborn may be due to :
 - a. Swallowed blood .
 - b. Hemorrhagic diseases of the newborn .

7. Renal functions :

- * Urination may be delayed for 24-72 hrs , depending on external atmospheric temp.
- * The kidney is not able to concentrate urine.
- * Urine may contain abundant urates which give the pink stain of urine.
- * ~~~ GFR is also present & may lead to retention of drugs and toxicity.

8. Genitalia & mammary glands :

- * Enlargement & secretions of the breasts in both sexes may occur.
- * Hypertrophy & enlargement of both labia may occur in females.
- * Both conditions are due to passage of maternal estrogen through the placenta.

9. Blood :

* Hb % : 17-19 gm % with mild reticulocytosis & normoblastemia.

* WBCs :

a. After the 1st 24hrs : 25000 / cmm with relative neutrophilia.

b. After one week : 15000 / cmm with relative lymphocytosis.

* Coagulation factors : There is little transfer of certain coagulation factors from the mother. Establishment of normal hemostatic mechanisms depends on early development of normal bacterial flora & elaboration of adequate amount of vit. K.

The post-term newborn

Definition

Baby delivered after 42 weeks of gestation regardless of birth weight.

Etiology

1. Idiopathic.
2. Chromosomal abnormalities.
3. Neural tube defects, because an intact fetal pituitary-adrenal axis is involved in initiation of labor.

Physical characteristics

1. He is alert, with open eyes.
2. The skin is pale, desquamated, wrinkled & dry.
3. Absent lanugo hairs.
4. Decreased or absent vernix caseosa.
5. Long nails.
6. ± Meconium staining.

Problems of post-maturity

The mortality rate is 3 times that of the term infants due to :

1. Congenital anomalies which may be the cause of post-maturity.

2. Meconium aspiration.
3. Persistent pulmonary hypertension.
4. Hypoglycemia, hypocalcemia, polycythemia.
5. Perinatal depression.

Management of the post-mature neonate.

Delivery of a post-term newborn should take place in an equipped hospital with a neonatal intensive care unit.

1. Routine delivery room & nursery care plus :
 - a. Resuscitation if needed.
 - b. Ante-, intra-, & post-partum monitoring of the fetal well being.
2. Management of the above mentioned complications

The large for gestational age newborn

Definition

Baby whose birth weight measures $> 90^{\text{th}}$ percentile (or $> 2 \text{ SD}$) for his calculated gestational age.

The LGA could be FT, PT, post-term.

Etiology

1. Constitutional (large parents).
2. Infant of diabetic mother.
3. All causes of hydrops fetalis.
4. Beckwith – Wiedmann \$.

Problems of LGA

1. Special problems related to the underlying cause .
2. Transient tachypnea of the newborn especially if born by C.S.
3. Birth injuries.
4. Hypoglycemia.(IDM, BW\$, Erythroblastosis fetalis).

Management of LGA

Delivery of a LGA newborn should take place in an equipped hospital with a neonatal intensive care unit.

1. Routine delivery room & nursery care plus :
 - a. Resuscitation if needed.
 - b. Ante-, intra-, & post-partum monitoring of the fetal well being.
2. Management of the above mentioned complications

Apgar Score

Measuring the score at $\Rightarrow$

1. 1 minute $\Rightarrow$ as indicator for the presence of asphyxia & helps to decide the needed mode of resuscitation.
2. 5 minutes $\Rightarrow$ is a more accurate indicator for later neurologic residual damage.

The following signs are observed & given a score 0, 1 or 2.

Score Sign	0	1	2
HR	Absent	< 100	>100
Respiration.	Absent	Slow & irrigrular	Good crying
Muscle tone	Absent	Some flexion of exremities	Active movements
Reflex to nasal catheter	Absent	Grimace	Cough, sneeze
Color	Blue or pale	Body pink & exremities blue	Completely pink

A. A score of 8-10

$\Rightarrow$ Indicates good general condition & no asphyxia.

1. Gently, suction air way including nares.
2. Good dryness of the baby including the head.
3. Maintain body temperature.

B. Ascore of 5 -7:

$\Rightarrow$ Indicates mild asphyxia

1. Stimulate breathing by repeated slapping of the soles, or rubbing of spine or sternum.
2. Provide O2 by bag & mask.
3. If the mother has received narcotics during labor $\Rightarrow$ Give 0.01mg / Kg IM

↓
If improving
↓

Continue as A

↓
If deteriorating
↓
Continue as C

C. A score of 3 - 4

$\Rightarrow$ Indicates moderate asphyxia.

1. Ventilate with bag & mask, using 100% O2, till improvement & spontaneous respiration begins.
2. If the heart rate is less than 60 $\Rightarrow$ intubate the baby & cardiac massage at a rate of 120/min is done.

D. A score of 0 -2:

⇒ Indicates severe asphyxia.

1. Proceed directly to intubation & bag ventilation with 100% O₂
2. Perform cardiac massage.
3. If no improvement within 2 minutes ⇒ insert umbilical catheter & give the following drugs.
 - a. NaHCO₃ ⇒ to correct metabolic acidosis.
 - b. Glucose 10-25% ⇒ to correct hypoglycemia.
 - c. Epinephrine 0.01mg/Kg IV or endotracheal & may be repeated every 5 minutes.
 - d. Finally ⇒ Ca-gluconate 1-2 ml/kg slowly IV.
- All these drugs are ineffective in absence of adequate O₂-ventilation.



Come on .. Let's gooooo

Neonatal Reflexes

Moro reflex

Stimulus

1. Making a loud noise near the ear.
2. Sudden withdrawal of the blankets from underneath the infant.
3. Sudden dropping of the head for about 15 in the examiners hand.
4. Putting a cold hand or stethoscope on the baby's skin.

It is produced by excitation of cervical or labyrinthine proprioceptors by movements.

Response.

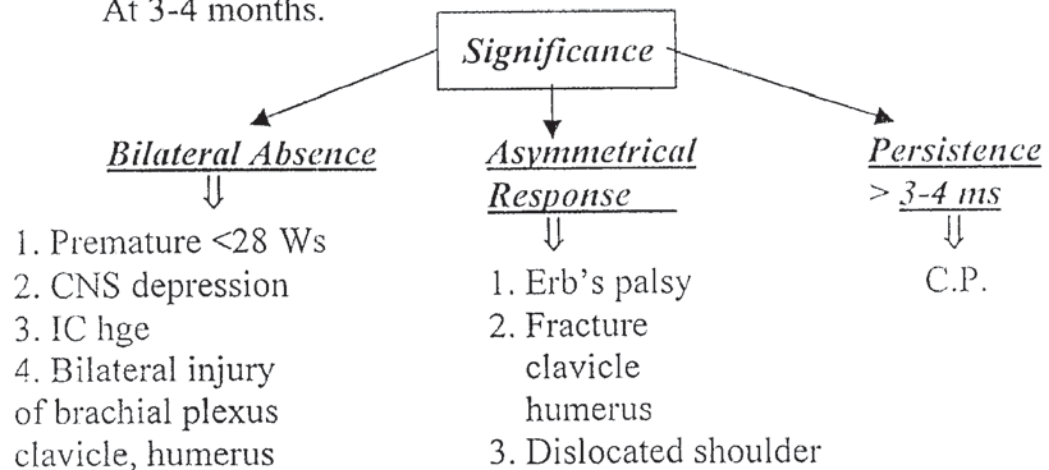
Extension of the trunk + Extension & abduction then flexion & adduction of the arms.

Age of appearance:

Birth (28 weeks)

Disappears.

At 3-4 months.



Placing Reflex

If the dorsum of foot touches the under edge of the table.

⇒ The foot is lifted and placed on the table.

Appearance : At birth.

Disappears : At 1 ½ months.

Absence : CNS depression or LL paresis.

Stepping reflex

If soles of feet touch the surface of the table in the erect position ⇒

Inclining the body forwards ⇒ Regular alternating steps forwards.

Appearance : At birth.

Disappears : At 1 ½ months.

Absence : CNS depression or LL paresis.

Rooting & suckling Reflexes

Stimulation of the cheek $\Rightarrow$ turning of the face & mouth towards the stimulus then stroking the lips $\Rightarrow$ Repeated suckling movements by the mouth.

Appearance : At birth.

Disappears : At 4 ms awake & 7 ms asleep.

Absence : CNS depression.

PT.

Bulbar palsy.

Grasp Reflex

Light touch to the palm of the hand $\Rightarrow$ the baby grasps

Appearance : At birth.

Disappears : Palmar at 6 ms & planter at 10 ms.

Absence : CNS depression .

Brachial plexus injury

Persistence : C.P.

Glabellar reflexes

Sharp tap on the glabella $\Rightarrow$ momentary tight closure of the eyes.

Appearance : 32-34 weeks.

Disappears : Variable.

Absence : CNS depression.

PT.

Pupillary Reflex

Close one eye & expose the other to light $\Rightarrow$ pupillary constriction.

Appearance : 29-37 weeks.

Disappears : Persists.

Absence : CNS depression.

PT.

Impaired vision.

Tonic neck reflex

Put the baby in supine position $\Rightarrow$ turn the head rapidly to one side $\Rightarrow$ Extension of limbs on the side to which the face is turned & flexion of limbs on the other side.

Appearance : At 2 ms.

Disappears : At 6-7 ms.

Absence : Medullary or spinal cord lesions.

Neck righting reflex

Put the baby in supine position $\Rightarrow$ turn the head slowly to one side $\Rightarrow$ Rotation of the trunk to the direction of the head.

Appearance : 32-34 weeks.

Disappears : 24 ms.

Absence : It is absent or decreased in infants with spasticity

Parachute reflex

If the infant is suspended in the prone position & suddenly allowed to fall for a short distance $\Rightarrow$ Extension of arms, hands & fingers occur. Appears at 9 ms & persist.

It is absent or decreased in infants with spasticity.

Landau reflex

If the infant is suspended in the prone position with the examiner's hands below the abdomen $\Rightarrow$ Extension of the head, trunk & hips. then flex the infant's head $\Rightarrow$ Flexion of the trunk & hips

Appears at 3 ms & disappears at 24 ms.

It is absent or decreased in infants with spasticity.

Other reflexes.

1. *Deep tendon reflexes* $\Rightarrow$ normally present at birth usually brisk.
2. *Babiniski sign* $\Rightarrow$ An extensor response is usually obtained during the 1st year of life.

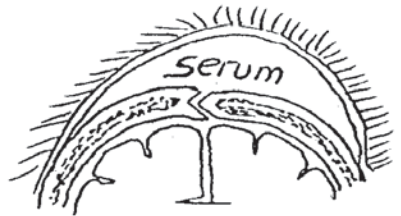


Birth Injuries

Head injuries

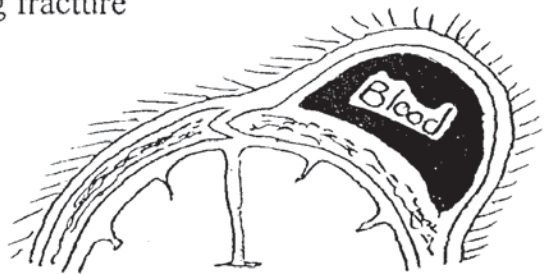
Caput Succedaneum

- It is diffuse edematous swelling of the soft tissues of the scalp involving the presenting part of the fetus at birth.
- It is maximum at birth & disappears gradually within few days.
- It crosses suture lines
- No t t t is needed.



Cephalhematoma.

- It is subperiosteal hge of the skull
- Characters
 1. It doesn't cross suture lines.
 2. It is not present at birth, then gradually develops within hours.
 3. No discoloration of the overlying skin as in caput succedaneum.
 4. In 25% $\Rightarrow$ there's an underlying fracture



Complications.

1. Anemia.
2. Hyper-bilirubinemia.
3. Infection.
4. Disfigurement of the skull
5. Organization with fibrosis & calcification.

Treatment

1. Depressed fracture $\Rightarrow$ Correction.
2. Shock or anemia $\Rightarrow$ Blood or packed RBCs transfusion.
3. Hyperbilirubinemia $\Rightarrow$ phototherapy or exchange transfusion.
4. Infection $\Rightarrow$ antibiotics & drainage of pus if formed.

Intracranial Hemorrhage.

Etiology

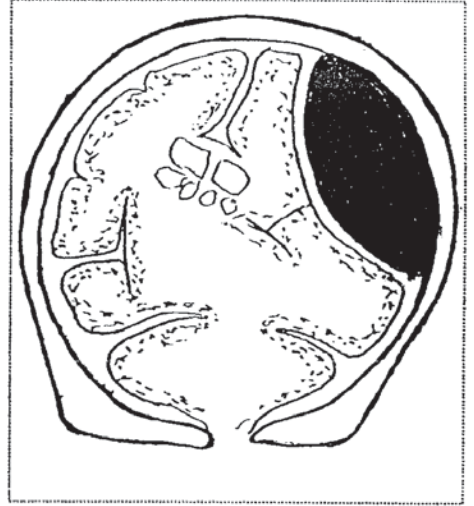
1. Trauma $\Rightarrow$ Forceps.
2. Anoxia.
3. Hgic blood disease.
4. Vascular anomalies.

5. Prematurity: in the PT the blood vessels lining the ventricles are fragile & have little support & also lack the normal autoregulation which copes with changes in the BP to maintain the cerebral perfusion.

C/P

It may present at birth or later on

1. Poor feeding.
2. Disturbed level of consciousness which may reach to coma.
3. Convulsions.
4. Absent moro reflex.
5. Central RD $\Rightarrow$ slow irregular respiration apnea & cyanosis.
6. Manifestations of $\uparrow$ ICP
 - Forceful vomiting.
 - High pitched cry
 - Convulsions & tense bulging fontanel
7. Eye signs $\Rightarrow$ unequal pupils
 - Failure to react to light.
 - Nystagmus
 - Retinal hge.



Investigations

1. Brain Sonar.
2. Brain CT-scan.
3. MRI

Treatment

A. Prevention.

1. Good obstetric care.
2. Prevention of prematurity.

B. Curative.

1. Incubator care.
 - a. Position of the newborn. $\Rightarrow$ Raise the head 30 degrees $\rightarrow$ why?
 - b. Tube feeding or IV-Fluids.
2. Convulsions.
 - $\Rightarrow$ Phenobarbitone.
3. Hgic blood diseases.
 - a. Vit K1 $\Rightarrow$ 1-5 mg IM
 - b. FFP or fresh blood

- c. 4. Surgical evacuation or tap. & if hydrocephalus develops
⇒ shunt operation.

Peripheral Nerve Injury

Erb's Paralysis

Etiology

Injury of C5 & C6

Position

The affected UL is:

1. Adducted & internally rotated at the shoulder
2. Extended at the elbow
3. Pronated forearm
4. Flexed at wrist.

Policeman's tip position

5. The paralyzed limb of LMNL i.e. hypotonia
Loss of biceps reflex " C5 & 6 "
Atrophied biceps.
Unilateral absent Moro-reflex.
6. The hand moves well
i.e. intact grasp reflex.
7. Sensory impairment on the outer aspect of the arm.



ttt

⇒ "Airplane- splint" ⇒ the arm is abducted 90 degree + external rotation at the shoulder + full supinated forearm + slight extension at the wrist for 1 week then start physiotherapy.

Klumpke's paralysis

Etiology

Injury of C7, C8 & T1

C/P

1. Paralysis of the muscles of the hand ⇒ loss of hand grip & grasp reflex.
2. Horner syndrome ⇒ is usually associated due to interruption of cervical sympathetic fibers in T-1
⇒ Ptosis, miosis, anhidrosis
& enophthalmos on the same side.

ttt

Intermittent padding of the fist with small ball & splinting the wrist in neutral position for 1 w then start physiotherapy

N.B.

If paralysis persist for 2-5 months neuroplasty is indicated.

Phrenic nerve paralysis

Etiology:

Injury of C 3,4 & 5.

C/P:

1. cyanosis & irregular respiration.
2. Breathing is thoracic in type > no bulging of the abdomen with inspiration.
3. Diminished air entry on the affected side.

Investigations:

Fluoroscopy : elevation of diaphragm on the paralyzed side during inspiration.

ttt

1. The infant should be placed on the paralyzed side.
2. O₂ is given if necessary.
3. Progressive naso-gastric tube feeding or IV fluids if severe RD.
4. Surgical plication is rarely indicated.

Facial Nerve Palsy

⇒ due to compression of the facial nerve by forceps delivery.

C/P

There is deviation of the mouth to healthy side, failure to close eye, absent naso-labial fold & feeding troubles due to buccinator paralysis.

ttt

1. Care of the eye & feeding.
2. Neurplasty ⇒ if paralysis > 3ms

Sternomastoid muscle injury

⇒ due to neck traction during delivery ⇒ hematoma of the sternomastoid ⇒ fibrosis ⇒ calcification ⇒ firm mass "Sternomastoid mass".

⇒ shortening of the ms ⇒ torticollis of the neck.

!!!

1. Physiotherapy.
2. Surgical release of the affected ms in case of failure of physiotherapy.

Visceral Injury

⇒ Due to rough manipulation during breech delivery.

- Subcapsular hematoma of the liver, rupture spleen & adrenal hge are the commonest.

⇒ severe pallor, jaundice, shock & palpable abdominal ms.

Low Birth Weight

Definitions

1. Low Birth weight "LBW"

Wt < 2.5 Kg at birth

2. Very Low Birth weight "VLBW"

Wt < 1.5 Kg at birth.

3. Preterm

Any live-born baby delivered before 37 weeks.

4. Small – For date

The birth weight is less than the 10th percentile for his calculated gestational age. "due to IUGR"

5. Post-term

Infant born after 42 weeks

Etiology

- A. Preterm delivery About 60% of cases.

1. Idiopathic : In 50% of cases.
2. Twin pregnancy.
3. Ante-partum Hge.
4. Toxemia.

5. Diabetic mother.
6. Premature separation of the placenta.
7. Badly timed C.S.

B. IUGR "Small-for-date" About 40% of cases.

1. Ante-natal infections: STORCH.
2. Congenital anomalies of the fetus.
3. Chromosomal aberrations.
4. Placental dysfunction syndrome
⇒ Fetal malnutrition.

How to differentiate between premature & IUGR?

⇒ By assessment & calculation of gestational age.

Assessment of gestational age

History

1. Date of LMP.
2. Date of onset of fetal movement "18-20 Ws"

Ante-natal examination.

Fundal level.

Ante-natal investigations.

1. U/S ⇒ Bi-parietal diameter.
Bi-acromial diameter.
2. Amniotic fluid analysis.
For lung ⇒ L/S ratio.
For kidney ⇒ Creatinine.

You can do it ...

At Birth

A. Physical Signs.

2. Ear cartilage

the helix & antihelix stand out between 36-40 weeks.

3. Size of breast nodule

- at 33 ws $\Rightarrow$ not palpable
- at 36 ws $\Rightarrow$ 3 mm
- at 40 ws $\Rightarrow$ 4-10 mm

5. Sole creases.

- 36 ws = only 1-2 creases.
- 37 -38 ws = more creases.
- 40 ws = criss-cross pattern covering the sole.

1. Scalp hair

- a. <37 ws $\Rightarrow$ short & fuzzy.
- b. At 40 ws $\Rightarrow$ coarse individual strands.

4. Genitalia

a. Female genitalia.

- 36 ws $\Rightarrow$ minora > majora
- 40 ws $\Rightarrow$ majora > minora

b. Male genitalia.

- 36ws $\Rightarrow$ few rugae & undescended testes.
- 40ws $\Rightarrow$ descended testes & rugae covering all the scrotum.

B. Neurologic evaluation.

1. Pupillary light reflex $\Rightarrow$ 29-31 ws.
2. Moro reflex $\Rightarrow$ 28-31 ws
3. Glabellar reflex $\Rightarrow$ 32-34 ws.
4. Rooting reflex $\Rightarrow$ 31-33 ws.
5. Suckling reflex $\Rightarrow$ 31-33 ws.

The Preterm Baby

Criteria of Prematurity

1. Birth wt $\Rightarrow$ < 2.5 Kg.
2. Length $\Rightarrow$ < 47 Cm.
3. Skull circumference $\Rightarrow$ < 33 Cm.
4. Chest circumference $\Rightarrow$ < 30 Cm.
5. Foot length $\Rightarrow$ < 7 Cm.
6. Absent ossific center in the cuboid bone.

Handicaps & Complication of prematurity

Respiratory.

1. Immature respiratory center $\Rightarrow$ irregular, periodic respiration & recurrent apnea.
2. $\downarrow$ Surfactant $\Rightarrow$ RDS.
3. Weak respiratory ms & weak thoracic cage.
4. Weak cough & gag reflexes $\Rightarrow$ aspirations.
5. Poor function of the cilia $\Rightarrow$ chest infection.
6. Immature pulmonary capillaries $\Rightarrow$ pulmonary hge.

Inadequate regulation of body temp.

1. Immature heat regulating system.
2. $\uparrow$ Surface area in relation to body wt.
3. $\downarrow$ S.C. Fat $\Rightarrow$ $\uparrow$ heat loss.
4. $\downarrow$ Ms. activity $\Rightarrow$ $\downarrow$ heat production.

Renal

1. $\downarrow$ GFR
2. Inability to concentrate urine.

Hepatic

1. Delayed activation of hepatic enzymes $\Rightarrow$ physiological jaundice.
2. $\downarrow$ storage capacity of the liver esp. for glycogen $\Rightarrow$ $\uparrow$ liability for hypoglycemia.

Hemostatic handicaps.

1. $\downarrow\downarrow$ clotting factors $\Rightarrow$ due to hepatic immaturity.
2. $\uparrow\uparrow$ capillary fragility $\Rightarrow$ due to inadequate supporting tissues.

CVS.

1. $\uparrow\uparrow$ shunting of blood through PDA & foramen ovale in response to hypoxia, stress & polycythemia $\Rightarrow$ circulatory insufficiency & under perfusion of vital organs.
2. Persistent P++ $\Rightarrow$ $\uparrow\uparrow$ blood shunting.

Immunologic handicaps.

1. Defective transfer of Igs "IgG".

2. Immature immune functions as phagocytosis, T-cell function, B-cell function & ↓↓ complement .So sepsis is more common.

CIT

1. Weak suckling & swallowing reflexes.
2. ↓ capacity of stomach & low gastric acidity.
3. ↓↓ bile salts ⇒ fat & fat soluble vitamins malabsorption.
4. Diminished body stores of minerals. & vitamins e.g. Iron & VitD.
5. Delayed neuro-muscular coordination. ⇒ freq. vomiting.

Complications of prematurity.

1. Respiratory.

- Hyaline Membrane Disease.
- Atelectasis ⇒ either 1ry or 2ry.
- Pulmonary hge.
- Recurrent apnea.

2. Hyperbilirubinemia & kernicterus.

3. IC- hge
4. Intercurrent infections ⇒ E-coli & staph.
5. Retro-lental fibroplasia.
⇒ due to prolonged use of O₂ at high tension .
6. Hypothermia.
7. Hypoglycemia.
8. NEC.
9. Persistent PDA.
10. High incidence of organic brain damage.
11. High incidence of rickets & iron-deficiency anemia.

*It's your own way ..
prove yourself*

Small-for date "Dysmature baby".

Physical character.

1. Muscle wasting due to intra-uterine malnutrition.
2. Skin $\Rightarrow$ thin loose, dry & cracked, with minimal S.C. fat.
3. Scalp hair $\Rightarrow$ sparse & may fall completely.
4. Widely opened fontanels & sutures.
5. The umbilical cord is very thin & may be meconium stained.

Complications

1. Perinatal asphyxia.
2. Hypoglycemia.
3. Hypothermia.
4. Pulmonary hge.
5. Meconium aspiration.
6. NEC.
7. Polycythemia.
8. Illness related to cong. anomalies or cong. infections.



We will always be with you

Management of LBW

Prevention.

Good ante-natal care is essential to avoid the preventable causes as:

1. Ante-natal STORCH infections.
2. Control of maternal diseases e.g. DM, hypertension etc.
3. Ante-natal care of maternal nutrition.
4. Avoid exposure to teratogens & irradiations.
5. Avoid unnecessary C.S.

Active t t t

I. Incubator care.

1. For regulation of body temp.
2. Regulation of relative humidity "40-60%.
3. Regulation of O₂ concentration.
4. Reduction of the possibility of contamination.

II. Feeding.

Onset $\Rightarrow$ as early as possible for fear of hypoglycemia.

Mode of feeding.

1. If he can suckle & swallow $\Rightarrow$ breast or bottle.
2. If he can swallow only $\Rightarrow$ breast milk by dropper or spoon.
3. If he can't suckle or swallow $\Rightarrow$ nasogastric tube feeding.
4. If there is respiratory distress, IC-hge, NEC & Other causes of intestinal obstruction $\Rightarrow$ I.V. fluid therapy.

Type of feed.

1. Breast milk of the preterm baby is more suitable than full term breast milk $\Rightarrow$ why?
2. Humanized milks are suitable for most infants.
3. Special preterm formula is available.

Amount of feed.

We start 5-10 ml / fed & $\uparrow$ gradually according to tolerance of feeding.

N.B.

Regurgitation, vomiting, abdominal distension or residual from the previous feed upon gastric suction $\Rightarrow$ suspicion of sepsis or NEC should be considered.

Fluid Requirements.

1. F.T. $\Rightarrow$ we start by 60 ml / kg in day "1" $\Rightarrow \uparrow$ 10-20 ml / kg / D till max. 150 ml / kg / D
2. PT $\Rightarrow$ 80ml / kg in day "1" $\Rightarrow \uparrow$ 10-20 ml/Kg / D till max 150 ml / kg /D.

III. Prevention of infections.

1. Every thing should be completely sterile.
 2. Prophylactic antibiotics.
Penicillin + Garamycin.
- Immunoglobulin preparations may be given.

IV. Prevention of nutritional disorders

1. Vit - K1 $\Rightarrow$
1-5 mg IM immediately after birth.
2. Vit-E $\Rightarrow$ to prevent hemolysis.
3. Vit - D, C & Iron should be started as early as 2nd month.



Happy Mother's Day

Increase your efforts ...

Neonatal Respiratory Distress

It may be due to

<i>Parameter</i>	<i>CNS-failure</i>	<i>Peripheral resp. diff</i>
Causes	1. Maternal narcosis 2. Perinatal anoxia 3. IC he. 4. CNS anomalies 5. Hypothermia 6. Hypoglycemia 7. Septicemia	<u>A. Pulmonary causes</u> 1. Idiopathic RDS 2. Iry atelectasis. 3. Aspiration of amniotic fluid. 4. Penumonia⇒ cong. Or acquired. 5. Pneumothorax. 6. Lobar emphysema. <u>B. Extra-pulmonary causes</u> 1. Choanal atresia. 2. Diaphragmatic hernia. 3. Tracheo-esophageal fistula. 4. Focal cord paralysis. 5. Laryngeomalacia.
C/P	1. Apnea 2. Slow, irregular, gasping respiration. 3. Cyanosis.	1. Tachypnea. 2. Working alae nasi 3. Expiratory grunting 4. Intercostal & subcost. retractions. 5. Chin tug. 6. Cyanosis.

Idiopathic Respiratory Distress Syndrome Hyaline Membrane Disease

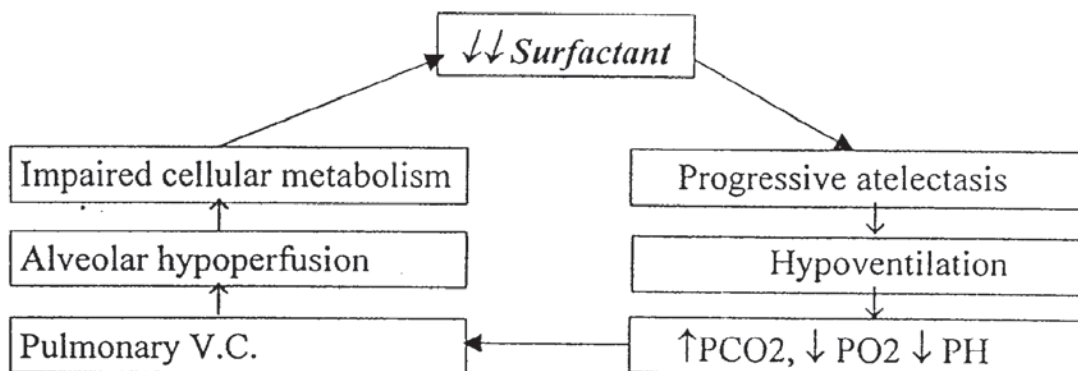
It is a major cause of neonatal death esp. in PT

Predisposing Factors

1. Prematurity.
2. Maternal DM.
3. C.S.
4. Perinatal anoxia.
5. Hypotention, hypovolemia & cold stress.

Etiology & Pathogenesis

- It is due to absence or deficiency of surfactant which is a phospholipid secreted by type II alveolar cells to line the alveoli.
- Surfactant $\Rightarrow$ $\downarrow\downarrow$ surface tension of the alveolar walls $\Rightarrow$ prevent alveolar collapse during expiration.
- In hyaline membrane disease "HMD": the following sequence occurs.



C/P

1. Tachypnea.
2. Working alae nasi
3. Expiratory grunting
4. Intercostal & subcostal retractions.
5. Chin tug.
6. Cyanosis.
7. Diminished air entry, fine & medium sized consonating crepitations on chest auscultation.

Investigations

1. CXR : reticulo-granular appearance.
2. Blood gases .
3. Shake test.

t t t

A. Prevention.

1. Avoidance or prevention of predisposing factors e.g.
 - a. Prematurity through appropriate management of high risk pregnancy & labor.
 - b. Avoidance of unnecessary C.S.

c. Careful management of diabetic mother.

2. I.U. Diagnosis & treatment.

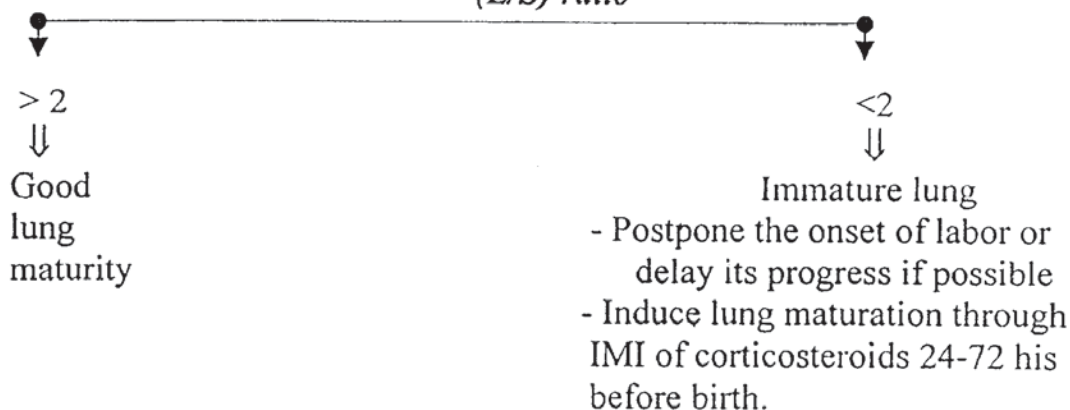
a. Calculation of gestational age through $\Rightarrow$ Date of LMP

U/S $\Rightarrow$ Skull diameter.

Bi-acromial diameter.

b. Amniotic fluid sample & measure lecithin / sphingomyelin

(L/S) ratio



3. Ante-natal & intrapartum monitoring of the baby to reduce the risk of fetal asphyxia.

4. Prevention of cold stress & birth asphyxia $\Rightarrow$ $\downarrow$ Risk of RDS.

B. Curative

- The ttt aims at breaking the vicious cycle mentioned before & supporting the newborn until he restarts to synthesize his own surfactant.
- Incubator care is usually necessary for prevention of hypothermia, O₂ administration, humidity & providing adequate IV fluids & nutrition are important.

1. Correction of hypoxia.

- Warm humidified O₂.
- Follow up by arterial blood gases.
- PO₂ should be kept at 60-80 mmHg
- If 70-100% O₂ is not sufficient to correct hypoxia $\Rightarrow$ Mechanical ventilator is indicated.
- Indications of assisted ventilation are :
 - a. pH < 7.2.
 - b. PCO₂ > 60 mmHg.
 - c. PO₂ < 50 mmHg at O₂ concentration of 70-100 %.
 - d. Persistent apnea.
- Q: Mention O₂ – toxicity ?

2. Correction of metabolic acidosis.

NaHCO₃ slowly IVI according to blood gases.

3. Antibiotics

- If infection occurs the appropriate antibiotic should be used.

4. Synthetic surfactant.

It is used as slow endo-tracheal administration through a special apparatus connected to the endotracheal tube.

5. Exchange transfusion.

May be used in ttt of RDS

⇒ Why?

6. General supportive care.

- Adequate nutrition.
- Prevention of hypothermia.

Complications of HMD & intensive care management

1. CNS : a. Central hypoxia.
b. Encephalopathy.
c. Intraventricular hge.
2. Complications of endotracheal intubation & ventilation :
a. Pneumothorax.
b. Pneumopericardium.
3. Complications of umbilical vessels catheterization :
a. Sepsis.
b. NEC.
c. Portal vein thrombosis.
4. O₂ toxicity :
a. Retinopathy.
b. Bronchopulmonary dysplasia.
5. Anemia due to frequent blood samples

Prognosis

Depends on early diagnosis and management in well equipped NICU by skilled personnel.

In good centers, about 50% of those under 1 kg survive and the morbidity progressively decreases at higher weights to over 95% in sick infants weighing more than 2.5 kg.

The long term prognosis for normal pulmonary function in most infants surviving HMD is excellent.

Transient tachypnea of the newborn RDS type II

Etiology

It is caused by delayed or slow absorption of fetal lung fluid.
- It is common in PT or FT who delivered by C.S.

C/P

1. Tachypnea of early onset may be the only finding.
2. Other sings of RD including grunting & cyanosis which are relieved by minimal O₂.
3. Recovery is usually rapid within 3 days.
4. Auscultation may show no crepitation or wheezes

Investigations.

CXR⇒ Prominent vasculature.
Fluid lines in lung fissures.

ttt

1. O₂ therapy
2. Stop oral feeding till tachypnea improves.



*We should help each other ..
It's one community*

Meconium aspiration syndrome

Risk factors:

1. Perinatal asphyxia.
2. Breech delivery.

hypoxia → relax of anal sphincter
passage of meconium

C/P:

1. Tachypnea.
2. Working alae nasi
3. Expiratory grunting
4. Intercostal & subcostal retractions.
5. Chin tug.
6. Cyanosis.

Investigations:

CXR ⇒ patches of lung collapse & over inflation.

t/t

1. Proper clearing of the airway by gentle suction may be life saving.
2. Gentle supportive therapy with minimal interference probably achieves the best results.
3. Supportive ventilation may aggravate the lung disorders.

& CPAP

Neonatal Apnea

Definition

It is cessation of breathing for more than 20 seconds or long enough to produce cyanosis & bradycardia

Etiology

1. Infections ⇒ Sepsis.
Meningitis.
NEC
2. CNS ⇒ Hge.
Kernicterus
Immaturity of respiratory center.
3. Respiratory ⇒ RDS
Severe pneumonia.
Pneumothorax.
Atelectasis.
4. Metabolic ⇒ Hypoglycemia.

Hypocalcemia.
Hypoxia.
Hypothermia.
Hypo & hypernatremia

5. GIT $\Rightarrow$ Gastro-esophageal reflux
NEC

ttt

1. Identification & ttt of the cause.
2. Stimulation of respiration by
 - a. Tactile stimulation of the skin.
 - b. Mask & bag may be needed.
 - c. Theophylline : IVI.
Loading $\Rightarrow$ 5mg/Kg
Maint $\Rightarrow$ 24 mg/Kg/D
3. Nasal CPAP $\Rightarrow$ may be needed if the previous measures fail.
4. Mechanical ventilation may be needed.

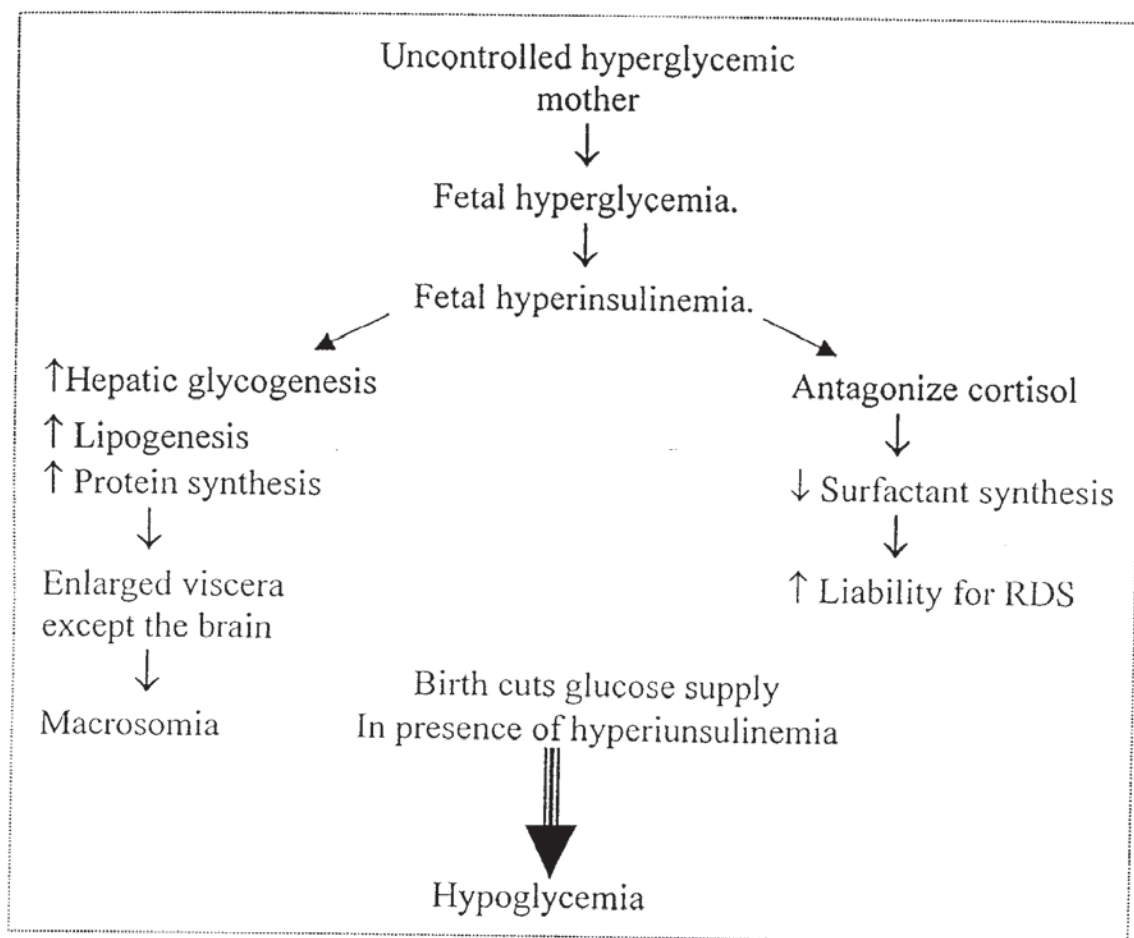


Make success your destiny

Infant of Diabetic Mother

It must be correctly called "Infant of a non controlled hyperglycemic diabetic mother".

Patho-Physiology



C/P

1. Large & plumpy ⇒ due to enlarged viscera.
2. Plethoric face ⇒ due to polycythemia.
3. Jitteriness or tremors, eye rolling even true convulsions.
4. Intermittent apnea spells or tachypnea.
5. Episodes of cyanosis.
6. Poor feeding.

*It's hard to win ..! but
it's better with this life*

N.B.

There is a high incidence of certain complication in addition to hypoglycemia

As:

1. RDS
2. Polycythemia.
3. Neonatal jaundice.
4. Hypocalcemia & hypomagnesemia.
5. Congenital anomalies.
6. HF
7. Severe hypoglycemia $\Rightarrow$ organic brain damage $\Rightarrow$ MR
8. Birth trauma $\Rightarrow$ due to macrosomia.

ttt

A. Before birth.

Careful efficient ante-natal care & good control of maternal diabetes.

B. After delivery.

1. Measurement of blood glucose every hour in the 1st 8hrs.
2. If clinically well with no hypoglycemia $\Rightarrow$ give early oral feeding every 2hrs.
3. If blood glucose < 35 mg/dl $\Rightarrow$ give IV infusion of glucose even if no symptoms.
4. Hypocalcemia $\Rightarrow$ 2-4 ml/kg calcium gluconate slow IV.
5. Hypomagnesemia $\Rightarrow$ Mg SO₄ 50% ml/kg.
6. ttt of other complications if present.



Be with us .. It's success

Neonatal Hypoglycemia

Definition

Neonatal hypoglycemia is defined as blood glucose

- * < 35 mg/dl during the first 3 hrs.
- * < 40 mg/dl between 3-24 hrs.
- * < 45 mg/dl after 24 hrs.

Etiology

A. Inadequate substrate or enzyme function :

1. Intra-uterine growth retardation.
2. Prematurity
3. Infant of toxemic mother.
4. Infant with placental abnormalities.

B. Hyperinsulinemia :

1. Infant of diabetic mother. *At fetal hyperglycemia*
2. Rh-incompatibility.
3. Islet cell hyperplasia. *insulinoma*
4. Beckwith Wiedmann \$.
5. Panhypopituitarism.

C. Increased metabolic needs:

1. RDS.
2. Perinatal asphyxia.
3. Polycythemia.
4. Hypothermia.
5. Systemic infections.
6. Congenital cyanotic heart diseases.
7. Infants with heart failure.

D. Inborn errors of metabolism:

1. Galactosemia.
2. Glycogen storage diseases.
3. Methyl malonic acidemia.

C/P

⇒ As infant of diabetic mother.

ttt

1. High risk infant with normal blood glucose ⇒ early oral feeding/2-3 hrs.
2. If oral feeding is not tolerated ⇒ give IV infusion of glucose.



Ok .. Do it ...

Neonatal Jaundice

Definition

It is yellowish discoloration of skin, conjunctiva & mucus membranes due to increased serum bilirubin above 7mg /dl.

Bilirubin Metabolism

See chronic hemolytic anemia

Etiology

A. 1st. day

1. Hemolytic diseases of the newborn until proved otherwise.
 - Rh incompatibility
 - ABO & other groups incompatibility
2. Ante-natal infections i.e. TORCH-EB

B. 2nd -3rd day.

1. Physiological jaundice.
2. Crigler-Najjar syndrome "familial non-hemolytic jaundice"
3. Ante-natal infections.

C. 3rd -7th day.

1. Neonatal sepsis.
2. Absorption of hematoma e.g.
 - Cephalhematoma, IC hge.
 - Subcapsular hematoma of the liver.
3. Hereditary spherocytosis & G6PDD
4. Ante-natal infections.

D. After the 1st week

1. Congenital biliary atresia.
2. Neonatal hepatitis.
3. Septicemia & infections.
4. Hereditary spherocytosis & elliptocytosis.
5. G-6-PD deficiency "after intake of oxidizing agent.
6. Breast milk jaundice.
7. Galactosemia.
8. Inspissated bile syndrome.
9. Synthetic vit. K injection
10. Choledocal cyst.

E. Persistent after the 1st month.

1. Congenital biliary atresia.
2. Neonatal hepatitis.
3. Hypothyroidism.
4. Intestinal obstruction.

5. Congenital infections.
6. Galactosemia.
7. Inspissated bile syndrome.

According to the type of hyperbilirubinemia

I. Unconjugated hyperbilirubinemia.

A. ↑↑ Production.

1. Hemolytic disease of the newborn.
2. Hemolytic anemias $\Rightarrow$ G-6 PD deficiency - spherocytosis - Alpha-thalassemia.
3. Synthetic Vit. K. $\Rightarrow$ in G-6 PD deficiency.
4. Extravasated blood $\Rightarrow$ cephalhematoma, IC hge - subcapsular hematoma of the liver. $\Rightarrow$ hemolysis of RBCs.
5. Polycythemia. $\Rightarrow$ Plethora (excess of blood) due to high RBC count.

B. Hepatic conjugation defect.

1. Physiological jaundice. (Immature GT)
2. Defective conjugation. (Defect of UGT1A1)
Crigler - Najjar syndrome
3. Inhibitors of conjugation $\Rightarrow$ Breast milk jaundice: due to progesterone "pass 2" from breast milk.
Lucey - Driscoll syndrome: milk protein intolerance.
4. ↑↑ Enterohepatic circulation $\Rightarrow$
Constipation.
Pyloric stenosis.
Intestinal obstruction.
Meconium plug.
Meconium ileus.

II. Conjugated hyperbilirubinemia.

Conjugated $> 20\%$ total

A. Obstruction of bile flow.

1. Congenital biliary atresia.
2. Inspissated bile syndrome.
3. Choledocal cyst.
4. Dubin Johnson & Rotor S. $\Rightarrow$ defect in excretion of conjugated bilirubin.

B. Hepatic cell injury.

1. Neonatal hepatitis.
2. STORCH infection.
3. Sepsis.
4. IEM $\Rightarrow$ Galactosemia.
Tyrosinemia.

Hemolytic diseases of the newborn

Erythroblastosis Fetalis

Hemolytic disease of the newborn (HDN) results from transplacental passage of maternal antibodies active against fetal RBCs $\Rightarrow$ hemolysis $\Rightarrow$ neonatal anemia & jaundice.

Rh iso-immunization

About 85% of the population are Rh+ve "DD or Dd"
While 15% are Rh-ve "dd"

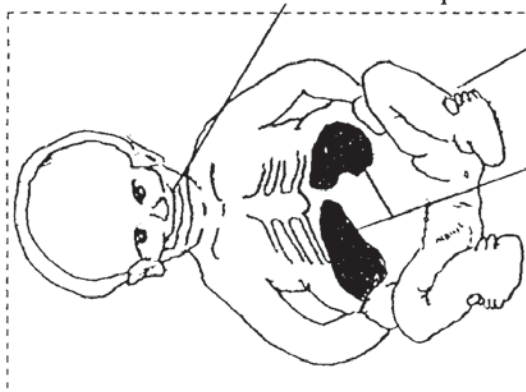
- If an Rh-ve mother gets pregnant with an Rh+ve baby $\Rightarrow$ Iso-immunization is liable to occur late in pregnancy or during labour or abortion due to escape of small amount of fetal blood (Rh+ve) to maternal circulation (Rh-ve).
- The same can occur if she receives Rh+ve blood transfusion.
- Rh isoimmunization is much less frequent inspite of high rate of Rh-ve mothers $\Rightarrow$ Why?

C/P

A. Hydrops Fetalis

This is the most severe form, due to severe intra-uterine hemolysis $\Rightarrow$ severe anemia & HF

1. The baby is born dead (SB) or die early after birth.
2. Marked pallor



3. Severe edema, pleural effusion & ascitis.

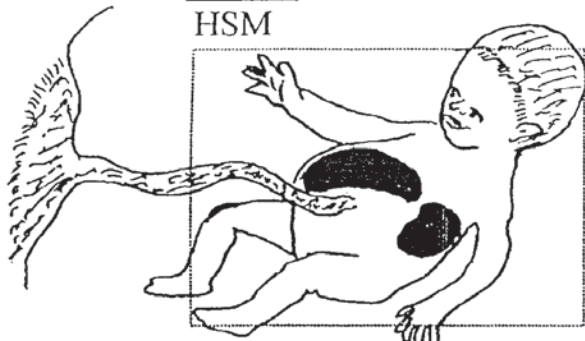
4. Huge HSM

5. Picture of circulatory collapse weak irregular pulse, failure to start respiration.

B. Icterus Gravis Neonatorum

1. Anemia at birth which worsen rapidly during the 1st day

HSM



Jaundice $\Rightarrow$ developing during the 1st few hrs & rapidly progressive.

* If not ttt early death occurs due to kernicterus or anemic HF

- Jaundice $\Rightarrow$ 1st $\Rightarrow$ hemolytic

Later $\Rightarrow$ obstructive “ inspissated bile \$”

C. Rh – Hemolytic Anemia

- In less severe cases.
- It is usually maximum at the end of the 3rd week.
- It may necessitate packed RBCs.

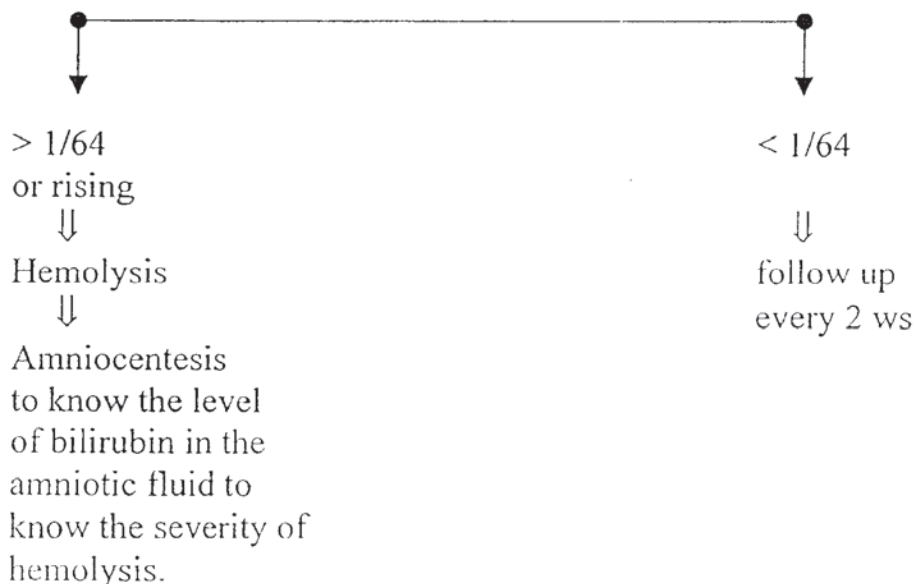
D. Very Mild Hemolysis.

- This may be detected only by lab. evidence of hemolysis.
- Otherwise the patient is normal.

Investigations

A. Ante-natal

1. Screening all females for Rh-ve persons.
2. During pregnancy
 - a. Measure maternal anti-D titre.



B. After Delivery

The cord blood is immediately analyzed for.

1. ABO & Rh group & compared to maternal blood group.
2. Hb & Hct $\Rightarrow$ if Hb < 14 = anemia.
3. S. bilirubin $\Rightarrow$ N. < 3 mg/dl
4. Retics.
5. +ve direct coomb's test.

ttt

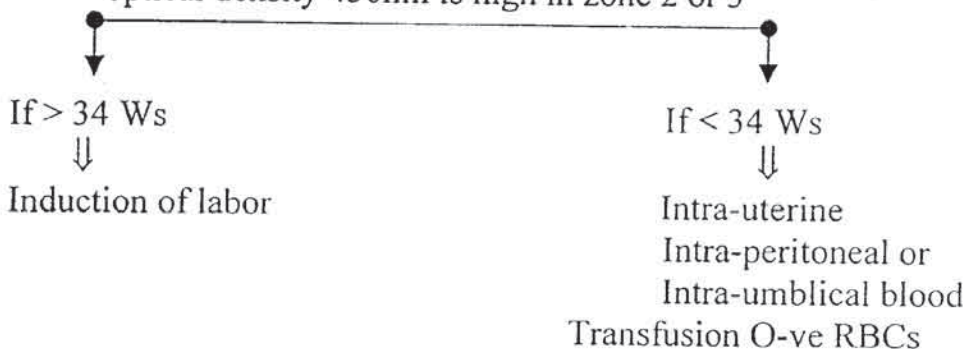
Prevention

1. Never give Rh+ve blood to Rh-ve female
2. Screening all females before marriage for Rh-blood group.
3. If Rh-ve female married to Rh+ve male
 $\Rightarrow$ Give anti-D gammaglobulin within 72hrs after birth or abortion.

Curative

A. Before birth

If spectrophotometric examination of amniotic fluid at the optical density 450nm is high in zone 2 or 3



B. After birth = ttt of hyperbilirubinemia

I. Exchange transfusion

- Aims $\Rightarrow$
1. Removal of excess bilirubin
 2. Correction of anemia.
 3. Removal of circulating anti-D

Indications

1. S. bilirubin $\Rightarrow$
 - a. In the cord > 5 mg/dl
 - b. Increasing 1mg/hr during the 1st 12 hrs
 - c. Near the critical level

18 mg	20mg/dl
$\Downarrow$	$\Downarrow$
PT	FT

2. Cord Hb 10gm/dl or less
3. At any sign of kernicterus.
4. History of previous neonatal deaths.

Type of blood given

1. If the blood is prepared before delivery $\Rightarrow$ O-ve blood.
Fresh
Compatible with maternal serum.
2. If prepared after delivery $\Rightarrow$ Rh-ve.
Fresh blood of the same ABO

Volume of exchanged blood.

$$= 85 \times 2 \times \text{wt (Kg)}$$

Expected effect

The serum bilirubin becomes about half the pre-exchange level.

- A rebound increase may occur within hours after exchange which may need another exchange transfusion.

Complications

- A. Immediate $\Rightarrow$
1. Hypoglycemia.
 2. Hypothermia.
 3. Hypocalcemia.
 4. Transient bradycardia with or without Ca infusion.
 5. Cyanosis.
 6. Transient vasospasm.
 7. Apnea.

- B. Late $\Rightarrow$
1. Inspissated bile syndrome.
 2. portal vein thrombosis.
 3. Infections: CMV, HIV, hepatitis.
 4. Graft versus host disease.

- Other indications of exchange transfusion.
 1. Neonatal septicemia.
 2. Neonatal polycythemia.
 3. Neonatal DIC
 4. Sickle cell anemia crises $\Rightarrow$ Partial exchange.
 5. Drug toxicity e.g. phenobarbitone.
 6. Metabolic diseases e.g. MSUD.

II. Phototherapy

Exposure to light especially in the blue zone $\Rightarrow$ converts the toxic unconjugated bilirubin into unconjugated isomers which can be excreted in bile & urine.

- It reduce serum bilirubin for about 1-3 mg/dl after 8-12 hrs of exposure

SO

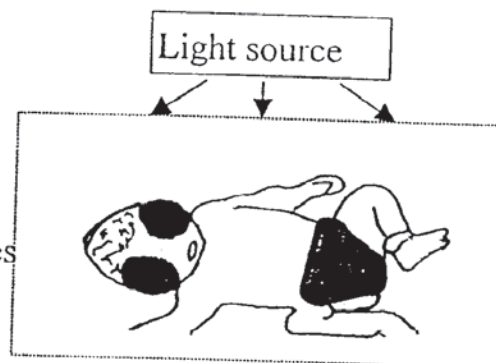
- It is unsuitable to replace exchange transfusion in the critical conditions.

- Eyes & genitalia must be covered.

Complications.

4Ds

1. Dermatitis.
2. Diarrhea.
3. Dehydration.
4. Damaging effect on retina & chromosomes
5. Bronzed baby \$ if applied to infant with direct hyperbilirubinemia.



III. Phenobarbitone.

$\Rightarrow \oplus$ Glucuronyl transferase enzyme.

Dose $\Rightarrow$ 3-8 mg /Kg/D even up to 10mg /Kg/D

IV. Packed RBCs

May be needed if anemia persist after disappearance of jaundice.

V. Hypoglycemia.

Commonly affects the newborn with Rh-incompatibility due to islet cell hyperplasia.

ttt $\Rightarrow$ see hypoglycemia.

ABO-Incompatibility

Although ABO incompatibility occurs in 25% of pregnancies $\Rightarrow$ hemolytic disease occurs in only less than 10% of such offspring due to

1. Low antigenicity of fetal ABO factors.
2. Maternal Abs are of the IgM $\Rightarrow$ doesn't cross the placenta

Character

1. The mother $\Rightarrow$ group O
Baby $\Rightarrow$ group A or B.
2. The 1st baby can be affected.
3. Onset of jaundice during the 1st 24 hrs but not at birth.
4. Mild course, mild anemia, mild HSM & less incidence of kernicterus.
5. Coombs test – ve or weak + ve.
6. Lab. findings.
 - Mild anemia.
 - Anti-A or anti-B can be detected in the baby's serum.
7. Photo-therapy may be enough in mild cases but exchange transfusion may be needed in severe cases.

Physiological Jaundice

- The most common.
- It affects 50% FT & more common & more severe in preterm "PT"

Etiology

1. Immature glucuronyl transferase enz.
2. Immature Z & Y-proteins "ligandin"
3. Short life span of RBCs $\Rightarrow$ $\uparrow\uparrow$ rate of destruction.

Character

1. Onset $\Rightarrow$ 2nd – 3rd day.
2. Disappears before 7th day.
3. In PT $\Rightarrow$ Earlier onset.
Reach higher peak.
Disappears before 14th D.
4. S. bilirubin doesn't rise over 10 mg/dl in FT & 14 mg/dl in PT it is of unconjugated type.

ttt

1. No ttt in mild cases.
2. Phototherapy & phenobarbitone are useful to prevent dangerous rise of unconjugated bilirubin.

It's the most God's important gift

Crigler - Najjar Syndrome

Due to congenital absence of glucuronyl transferase enzyme.

Type I (AR)

1. Complete absence
- ⇓
2. Severe jaundice
- ⇓
3. Kernicterus
- ⇓
4. Early death

Type II (AD)

1. Partial deficiency
- ⇓
2. Mild jaundice
- ⇓
3. Good response to phenobarbitone

Breast Milk Jaundice

Progesterone $\Rightarrow$ 3 α 20 β - pregnandiol $\Rightarrow$ secreted in milk $\Rightarrow$
 $\ominus$ Glucuronyl transferase enz.

ttt

Stop breast feeding for only 48 hrs $\Rightarrow$ then continue it again.

N.B. In Lucy Driscoll's the inhibiting substance is not identified.



It's motherhood ...

Cong. biliary atresia.

The most common cause of obstructive jaundice in the neonatal period.



C/P

1. Onset $\Rightarrow$ 2nd week.
2. Course $\Rightarrow$ progressive
3. Obstructive type
 - a. Urine $\Rightarrow$ dark
 - b. Stool $\Rightarrow$ pale "clay colored"
 - c. Olive green discoloration of skin & sclera.
4. Progressive hepatomegaly $\Rightarrow$ deterioration of liver functions.
5. Portal hypertension, ascitis, bleeding tendency & death due to liver cell failure.

Investigations

See neonatal hepatitis.

ttt

1. Extra-hepatic $\Rightarrow$ surgical
2. Medical care of the baby nutrition
 - a. Medium chain triglyceride instead of fat.
 - b. Fat soluble vitamins should be given by injection "Vit. A,D, K, E"
3. Management of liver cirrhosis & liver cell failure.

Neonatal Hepatitis

Etiology

1. Idiopathic
2. Infections
 - a. Viruses $\Rightarrow$ Hepatitis B or C
CMV
Herpes simplex
EBV
Rubella

- b. Bacteria ⇒ Septicemia
Portal pyemia.
Cong syphilis.
- c. Protozoa ⇒ Toxoplasmosis

C/P

Very similar to biliary atresia

Investigations

See the following table .

ttt

Bacterial ⇒ Antibiotics according to culture & sensitivity.

Viral ⇒ Acyclovir, interferon.

Toxoplasmosis ⇒ Daraprim or tripple sulpha.

<i>Investigations</i>	<i>Biliary Atresia</i>	<i>Neonatal hepatitis</i>
S. Bilirubin SGOT, SGPT Alk phosphatase..	↑↑↑ Direct ↑ Mild ↑↑↑ Marked.	↑↑↑ Biphasic ↑↑↑ Marked ↑ Mild.
U/S	1. Extrahepatic ⇒ dilated intrahepatic ducts 2. Intrahepatic ⇒ absent bile ducts.	Both intra& extrahepatic bile ducts are present.
HIDA scan	*Rapid hepatic uptake *Absent excretion into intestine..	• Poor uptake by the liver cells • Excretion into the intestine occurs
Liver biopsy	As U/S	• Infiltration by infla- mmatory cells + distor- tion of lobular architecture. • Bile ducts are present..

It's time to work hard

Kernicterus

Definition

Yellowish staining of certain brain nuclei especially the basal ganglia in the newborn as a result of high serum indirect bilirubin
⇒ neuronal necrosis ⇒ replaced by glial cells.

Etiology

- Neonatal indirect hyperbilirubinemia due to any cause may lead to kern-icterus.
- Serum bilirubin should rise above certain level.
- This level is determined by the maturity & vitality of the blood brain barrier "BBB"
- In FT = BBB is immature so the level is lower.
- Certain conditions further increase the incidence of kernicterus due to.
 1. ↑↑ susceptibility of CNS to the toxic effect of bilirubin.
 2. Affects the BBB
 3. Compete with bilirubin for its albumin binding sites.

e.g.

- a. Hypoglycemia.
- b. Hypoxia.
- c. Acidosis.
- d. Hypothermia.
- e. Sepsis & sulfa.

C/P

Stage I

Poor moro reflex.
Hypotonia
Lethargy
Poor feeding
Vomiting.
High pitched cry.

Stage II

Opisthotonus
Convulsions.
Rigidity.
Oculogyric crises.

Stage III.

The rigidity disappears & the general condition improves.

Stage IV

C P, deafness, choreoathetosis, MR.

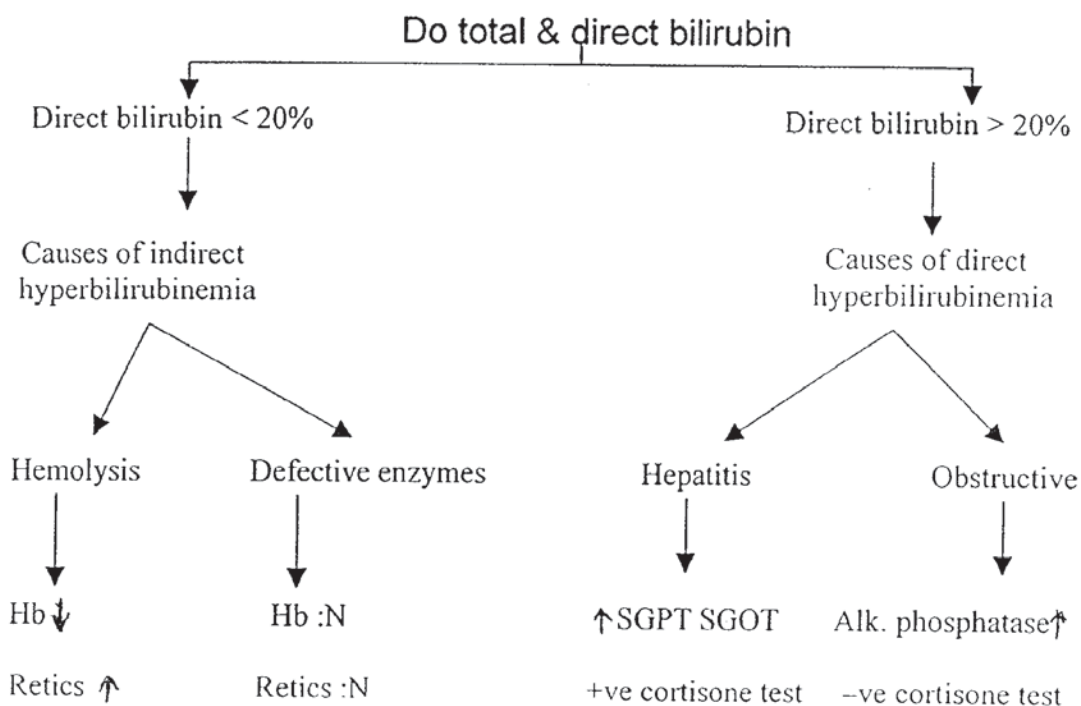
Investigations

Of neonatal jaundice.

ttt

- Prevention & ttt of indirect hyperbilirubinemia.
- Prevention & proper management of factors which $\uparrow\uparrow$ bilirubin toxicity.

How to investigate a case of neonatal hyperbilirubinemia



Hemorrhagic Disease of the newborn

It is spontaneous bleeding tendency affecting the newborns & preterms from the 2nd to 6th day of life.

Etiology

1. Vit. K deficiency $\Rightarrow$ due to absence of intestinal flora at birth.
2. Maternal deficiency of Vit. K.
3. Immaturity of the liver $\Rightarrow \downarrow\downarrow$ clotting Factors
4. Increased capillary fragility (in preterms).

Sites of hge.

GIT, nose, umbilical stump intracranial, pulmonary.

Investigations

1. $\uparrow\uparrow$ PT
2. BT $\Rightarrow$ N.
3. PTT $\Rightarrow$ N
4. $\downarrow\downarrow$ Factors II, VII, IX, X.
5. CBC $\Rightarrow$ normal platelet count.

Prevention

1. Give the mother $\Rightarrow$ 5-10 mg Vit K, IM 4-6 hrs before delivery.
2. Give the newborn $\Rightarrow$ 1mg Vit K1, IM immediately after birth.

ttt

1. Vit. K1 $\Rightarrow$ 1-5 mg IM or IV
2. Blood transfusion (Fresh whole blood) or FFP $\Rightarrow$ in severe cases.

D.D. of hge in the newborn

A. Hemophilias, A, B, C & Von Willibrand disease.

$\Rightarrow$ See hematology.

B. DIC : usually as a complication of sepsis, anoxia or acidosis.

⇒ See hematology.

C. Thrombocytopenia :

1. Isoimmune thrombocytopenia.
2. Maternal ITP.
3. Maternal SLE.
4. TAR S.
5. STORCII infection.
6. Neonatal sepsis.

C. Swallowed blood :

The infant may swallow the mother's blood during delivery or from a fissure in her nipple. Later blood is passed in the stool or is vomited.

In this condition alkaline denaturation test is essential to differentiate maternal blood from fetal blood.

Clinical evaluation	Laboratory studies			Diagnosis
	Platelets	PT	PTT	
<i>Sick</i>	↓	↑	↑	DIC
	↓	N	N	Thrombocytopenia
	N	↑	↑	Liver disease
	N	N	N	Vascular causes as in hypoxia , acidosis & premature
<i>Healthy</i>	↓	N	N	Immune thrombocytopenia & BM hypoplasia
	N	↑	N	Hemorrhagic diseases of the newborn
	N	N	↑	Hemophilia
	N	N	N	Bleeding due to local factor

Cyanosis in the Newborn

Etiology

A. Respiratory distress

Peripheral

1. RDS
2. Aspiration of amniotic fluid
3. Pneumonia
3. Atelectasis

Central

1. IC hge
2. Narcotics
3. Perinatal anoxia

B. Congenital cyanotic HD

1. TGA
2. Single ventricle
3. "Truncus arteriosus
4. Pulmonary atresia.
5. Severe F4

C. Methemoglobinemia.

D. Metabolic

- Hypoglycemia.
- Septicemia.
- Hypothermia.

Anemia in the newborn

It is usually physiological or pathological caused by :

1. Hemolysis
2. Hemorrhage.
3. BM depression.

Etiology

A. physiological anemia of the newborn:

1. Physiologic anemia of infancy:

After birth , there is rapid fall in Hb level , starting by the end of the 1st week of life and progressively declining reaching a lowest level at 6-8 weeks after birth . this a physiological phenomena called physiologic anemia of infancy and this is due to :

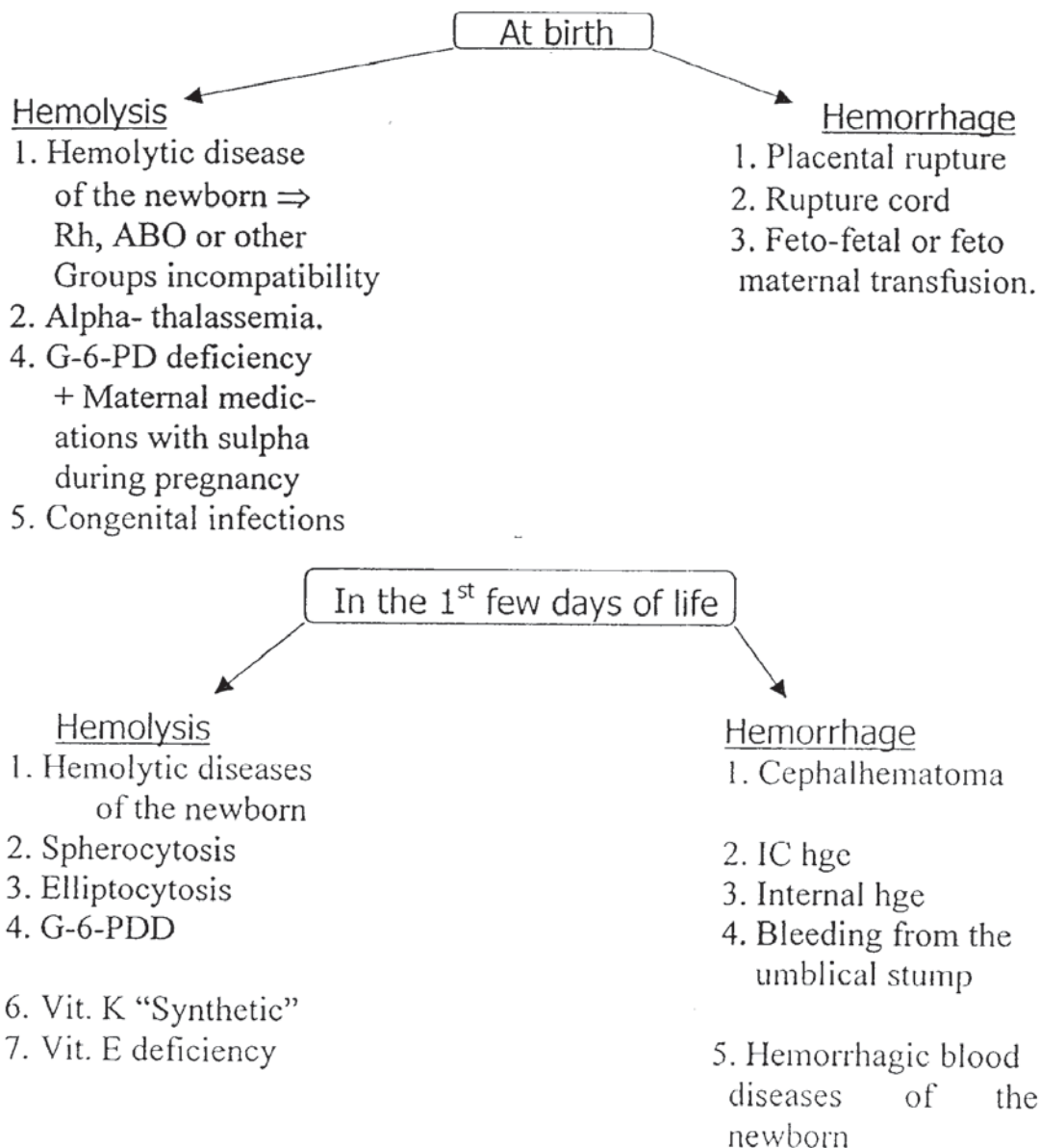
1. Shorter life span of the RBCs containing the fetal Hb.
2. Abrupt cessation of erythropoietin at birth as a result of onset of respiration and increased O₂ saturation.

Once the lowest level is reached , RBCs production is stimulated with gradual increase in Hb .

3. Anemia of prematurity:

It is an exaggeration of the normal physiological anemia . In addition , small premature infants develop rapidly vit. E deficiency unless supplied exogenously. Such vit. E deficiency causes more shortening of the life span of RBCs.

B. Pathological anemias in the neonatal period



Iatrogenic

Repeated blood sample

Investigations

1. CBCs & reticulocytic count.
2. Coomb's test.
3. G-6-PD assay.

4. Osmotic fragility test.
5. STORCH-EB screening.

ttt

1. ttt of underlying cause.
2. Packed RBCs transfusion if Hb < 10 gm%.
3. Recombinant human erythropoietin .

Fever in the newborn

- 2 important causes of fever in the neonate $\Rightarrow$ Dehydration fever
Neonatal infections

Dehydration fever

The most common cause of fever in the neonatal period

Etiology

1. Delayed feeding due to delayed breast milk production without fluid supplementation.
2. Exposure to high environmental temp.
3. Over-clothing especially in hot weather.

C/P

1. High body temp. (may be 40)
2. Hot dry, flushed skin.
3. C/P of dehydration depressed anterior fontanel, sunken eyes dry mucus membranes, dry tongue thirst & oliguria.
4. Convulsions may occur due to?

ttt

1. Correction of dehydration.
2. The condition is better prevented by early feeding of the baby.
3. Fluid supplementation is required esp. in hot weather.

Neonatal Infections

The infections of the newborn are discussed later in the notebook of infection.

Maternal diseases affecting the newborn

A. Infections

See neonatal infections .

B. Non-infectious diseases

1. Maternal Diabetes

- * Prematurity
- * RDS
- * neonatal hypoglycemia.
- * Macrosomia $\Rightarrow$ birth trauma

2. Toxemia, hypertension, renal disease.

- $\Rightarrow$
- * IURG $\Rightarrow$ small for date.
 - * Prematurity.
 - * IUFD

3. Autoimmune disease mediated by Ig G: SLE, myasthenia gravis. ITP & grave's disease.

4. Maternal PKU

- * Microcephaly
- * MR
- * Abortion
- * Small for date.

5. Osteomalacia.

- * Hypocalcemia.
- * Rickets.

Nonatal Convulsion

Etiology

1. Cerebral malformations, trauma, hge or anoxia.
2. Infections.
 - * Cerebral $\Rightarrow$ meningitis, encephalitis.
 - * Septicemia.
 - * Tetanus neonatorum.
3. Metabolic.
 - * Hypoglycemia.

- * Hypocalcemia.
 - * Hypomagnesemia.
 - * Hyper-natremia.
 - * Vit. B6 deficiency.
 - * IEM $\Rightarrow$ Galactosemia, MSUD
4. Toxins.
- * Drugs $\Rightarrow$ minophylline, coramine.
 - * Metabolic toxins.
 - Bilirubin $\Rightarrow$ kernicterus.
 - Uremic toxins.

Investigations.

To reach the cause

1. CBC + CRP $\Rightarrow$ for infections.
2. CSF examination.
3. Brain sonar.
4. Electrolytes + bilirubin + renal function.

ttt

- 1, Assurance of patent airway + O₂
2. Control of convulsions by:
 - a. Phenobarbitone.
 - 5mg/ kg IM
 - Can be repeated after 30 min.
 - b. Diazepam "valium"
 - 0.1 – 0.3 mg/kg IV
3. TTT of the cause.



Now .. We're the best

Edema in the Newborn

A. Generalized

1. Severe hemolytic disease of the newborn.
2. HF $\Rightarrow$ due to congenital HD
3. Congenital nephrotic syndrome.

B. Localized

1. Caput succedaneum.
2. Cord around the neck.
3. Congenital lymphedema.
4. Turner syndrome.



Till next time ...

Routine Care of The Neonate at Birth and Neonatal Resuscitation

- 1) The newly born baby is gently dried and wrapped in a warm, sterile towel.
- 2) The time of birth is noted.
- 3) Put the baby on a radiant warmer on his back with the neck in the neutral position (neither flexed nor extended to avoid airway compression) by putting a towel beneath the baby's shoulders.



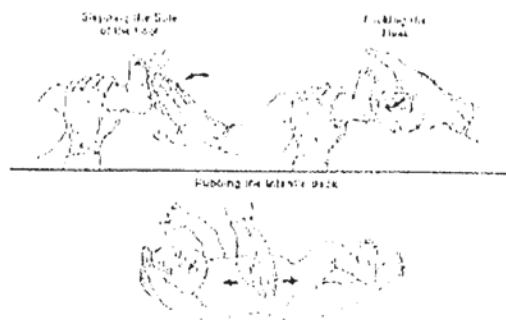
- 4) The upper airway is cleared by gentle suction of excess fluid and any inhaled vernix, blood or meconium: start by suctioning the mouth and pharynx since nasal stimulation by the suction catheter can induce a strong gasp with aspiration of oral and pharyngeal contents. Avoid too deep suctioning of the pharynx since this will induce vagal stimulation and bradycardia.
- 5) If the baby starts to breathe regularly with his color changing to pink no further resuscitative steps are needed. If not look at step (7).
- 6) Complete routine care by:
 - The umbilical cord is clamped and cut with sterile blades and the stump is cleaned with 70% alcohol and the entire skin is cleaned with sterile cotton soaked in mild soap solution.
 - Vitamin K: 1 mg IM is given to avoid hemorrhagic disease of the newborn
 - The baby is weighed and rapid clinical examination is done.
 - Care of the eyes is done by application of silver nitrate 1% or chloramphenicol eye drops.
 - The baby is dressed and put in the arms of his mother. The latter should be encouraged to put her baby as early as possible on her breast so as to enhance maternal neonatal bonding by early skin-to-skin contact.
- 7) If the baby is taking regular breaths but his color remains cyanotic he is in



need for additional oxygen by facemask till color improves.

8) If the baby fails in taking regular breaths or remains apneic do

a) Gentle stimulation by rubbing the back or slapping the soles of the feet.



b) In many cases blowing oxygen on the nose will initiate breathing.

c) If all of these steps fail the next step is to:

- i- Expand and ventilate the lungs with either bag and mask or bag and endotracheal tube. Often inflation of the lungs itself will initiate a gasp with spontaneous breathing. If it does not, the lungs should be ventilated at a rate between 30 and 50 inflations per minute with pressures below 30 cm H₂O. The majority of infants will quickly become pink and begin breathing within 2-5 minutes.



- ii- If the infant fails to become pink with good expansion of the lung then he is probably in a state of shock. Cardiac massage using two-finger pressure on the lower half of the sternum at a rate of 140 taps per minute is occasionally necessary.



- iii- Correction of acidosis by alkali injection, and persisting bradycardia by adrenaline administration into the umbilical vein can be helpful. If no improvement rapid intravascular expansion is done.

To summarize:

- Resuscitation is an orderly process which is done step by step whenever a neonate is in need for it depending on the color, breathing pattern and heart rate of the baby.
- Resuscitation steps are summarized by the letters ABCDE
 - A $\Rightarrow$ Airway which should be suctioned, cleared and opened by proper positioning of the head.
 - B $\Rightarrow$ Breathing which is stimulated by
 - Tactile stimulation
 - Blowing O₂ in the nose
 - Bag and mask ventilation
 - Ventilation by bag and endotracheal tube
 - C $\Rightarrow$ Circulatory support by cardiac massage in case of persistence of cyanosis and/or bradycardia in spite of proper chest expansion.
 - D $\Rightarrow$ Drugs used in resuscitation include:
 - Adrenaline (1/10.000 solution) 0.2 ml / Kg give either IV or via endotracheal tube and can be repeated
 - Sodium bicarbonate (8.4%) 2 ml / Kg = 2 mEq/Kg diluted 1:1 in glucose 5%.
 - Naloxone (Narcan) 0.1 mg/Kg/dose give IV, IM or via endotracheal tube if opiate narcotics were given to the mother in the past 4 hours.
 - Volume expanders given in case of shock as 20 ml/Kg of normal saline 0.9% or Ringer's solution or 10 ml/Kg of packed RBCs (in case of severe hydrops with heart failure).
 - E $\Rightarrow$ Evaluation of the success of the step or maneuver done in the resuscitation.
- APGAR score (named so according to Dr. Virginia Apgar, an American anesthetist) is a practical method which was used before for systematically assessing the newborn infant immediately after birth, at the 1st minute of life and thereafter depending on 5 objective signs (see table), but waiting till 1 minute to start inflation of the lungs whenever needed represent a lengthy delay in a life saving maneuver.

NEONATAL SCREENING

Definition:

Screening can be defined as the search for occult disease or the potential for disease to develop, in a defined population.

Aim:

The purpose is primarily to screen all newborn infants for a given disorder in which symptoms would not be clinically present until irreversible damage occurred and for which an effective treatment is available.

Timing:

Neonatal screening tests include a group of assays, which are carried out between the 3rd and 6th days of life, and become an essential measure for early detection of some inborn genetic defects.

Screening tests characteristics:

- The disease should be serious and common enough to warrant the effort and mass screening
- Early detection of the disease should be beneficial in terms of ease of treatment and improved prognosis
- The neonate should be normal at birth
- Follow-up mechanisms must be available.
- The screening tests must be easy to perform and interpret, and have acceptably low risk morbidity and cost with high sensitivity and specificity.

Neonatal screening for various disorders:

1- Clinical neonatal screening

- Congenital heart disease
- Congenital dislocation of the hip
- Tracheo-oesophageal fistula
- Imperforate anus

2- Neonatal screening for inborn errors of metabolism

Some examples are listed in the following table.

Disorder	Frequency	Mode of inheritance	Clinical picture
Phenylketonuria	1:14000	AR	Irreversible MR
Galactosemia	1:60000	AR	Vomiting, diarrhea, jaundice and failure to thrive, cataract in early infancy
Maple syrup urine disease	1:200000	AR	Severe acidosis, hypoglycemia, seizures, maple syrup odor
Homocystinuria	1:200000	AR	Marfanoid appearance
Hereditary fructose intolerance	1:20000	AR	Acute hypoglycemia, chronic hepatic & renal dysfunction

3- Neonatal screening for endocrine disorders

a- Congenital hypothyroidism

- The incidence has been estimated to be 1 in 4000 births
- Routine newborn screening in USA, Canada, most western countries and recently established in Egypt
- Carried out in dried spot samples collected via skin puncture obtained at 3-5 days after birth.
- T4 is measured initially, about 34% of low T4 values detected are not the result of true hypothyroidism, but represent diminished levels of thyroxin binding globulin (TBG).
- If the initial T4 is low, repeat T4 and TSH on the same sample with radioimmunoassay or with delayed fluorescence-immunoassay.
- If the repeated T4 is still low (< 6 microgm / dl) or the TSH is elevated, confirmatory serum sample should be obtained.
- Newborn infants with concurrent illness or congenital malformation may have transient TSH elevation. So re-evaluation of the diagnosis of congenital hypothyroidism in such infants is indicated.

b- Congenital adrenal hyperplasia

- The incidence of the classic form of this disorder varies from 1: 5000 to 1: 20000 depending in the population.
- Deficiency of 21 hydroxylase activity accounts or more than 90% of cases.
- Clinical diagnosis of 21-OH-D-CAH is poor in the neonatal period as clinical features range from classic salt-losing virilizing form to simple virilizing picture characterized by premature pubarche.

4- Neonatal screening for blood diseases

a- Screening for hemoglobinopathies

- i. Sickle cell disease
- ii. Hemoglobin e
- iii. Hemoglobin F

b- Screening for G6PD deficiency

5- Other disorders considered for neonatal screening

- a- Cystic fibrosis
- b- Alpha-1 antitrypsin deficiency
- c- Duchenne muscular dystrophy
- d- Neuroblastoma
- e- Familial ureteric reflux
- f- Liver diseases and biliary atresia
- g- Neonatal hearing screening
- h- Screening for congenital infections

Hypoxic – Ischemic Encephalopathy

Etiology

A. Fetal hypoxia

1. Maternal hypoventilation

- During anesthesia
- HF
- Carbon monoxide poisoning

2. Maternal hypotension

- Spinal anesthesia
- Compression of IVC & Aorta by the uterus
- Dehydration

3. Compression of umbilical cord impeding circulation of blood.

4. Uterine causes

- uterine tetany $\Rightarrow$ due to excessive oxytocin dose

5. Placental causes

- Premature separation
- Placental insufficiency.

B. Neonatal hypoxia

1. Severe anemia: Hemolysis

hge

2. Shock: Adrenal hge

IC hge

Infection

3. CNS depression: Narcotics

Injury

4. Pulmonary: RDS

5. Cong. Cyanotic heart disease.

C/P

1. IUGR due to fetal hypoxia
2. fetal heart rate slows & beat to beat variability declines.
3. fetal scalp blood analysis $PH < 7.2$
4. Meconium stained AF = fetal distress
5. At birth $\Rightarrow$ there's marked CNS depression with failure of spontaneous respiration
6. During resuscitation there's severe hypotonia which may change rapidly to hypertonia or normal tone.
7. Pallor, Cyanosis, apnea & slow HR.
8. Cerebral edema develops during the 1st 24hrs. $\Rightarrow$ severe brain stem depression.
9. Convulsions may occur & may be resistant to anticonvulsant therapy.
 $\rightarrow$ causes of convulsions are?
10. Disturbed level of consciousness.

Management

1. Avoidance of the causes of possible.
2. Monitoring of fetal wellbeing during pregnancy & labor.
3. Resuscitation
4. ttt of meconium aspiration .

Post-natal management

Investigations

- | | |
|--------------|-------------------------|
| 1. EEG | 5- ABG |
| 2. Brain U/S | 6- Renal function tests |

3. CT scan.
4. Creatine Kinase.

Treatment

1. O₂ level should be corrected by O₂ therapy.
2. Dobutamine $\Rightarrow$ to improve perfusion.
3. Correction of associated metabolic disorders $\Rightarrow$
 - hypoglycemia
 - Hypocalcemia
 - hypomagnesemia
4. Control of convulsions.

Prognosis

1. Death 10-20 % of infants.
2. C.P 20-45%
3. No brain damage 30-35%.

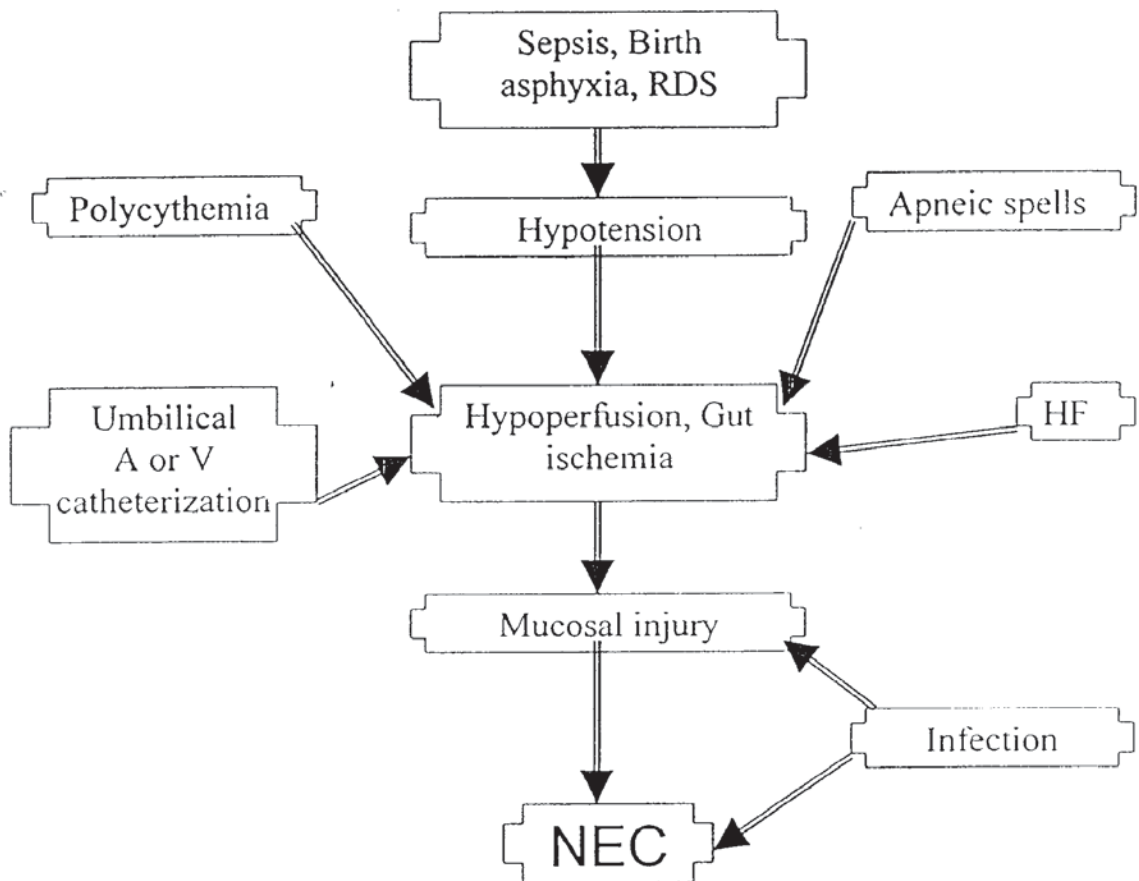


Please... give me it

Necrotizing Enterocolitis (NEC)

The disease commonly affects the ileum & colon but no part of the GIT is excluded

Etiology & Pathogenesis



C/P

NEC should be expected as a very probable complication in P.T. especially if there's predisposing factors.

I. Abdominal manifestations:

1. Abdominal distension.
2. Delayed gastric emptying.
3. vomiting which may be bilious.
4. bleeding/rectum & hematemesis may occur.
5. O/E → marked abdominal tenderness.

II. Systemic manifestations

1. Respiratory distress, Apnea.
2. Temperature instability.
3. Hypotension & shock
4. Bleeding tendency.

Investigations.

1. CBC: ⇒ Thrombocytopenia
2. Blood gases ⇒ persistent metabolic acidosis.
3. Refractory hyponatremia 1,2 & 3 are important triad in NEC.
4. Stool ⇒ blood in stool.
5. Plain X-ray erect abdomen ⇒ Pneumo-peritoneum

Management

- No oral feeding
- Nasogastric tube suctioning
- Begin parenteral feeding through peripheral vein.
- Treat any predisposing cause or complications as →

1. Infections

According to culture & sensitivity if the result not obtained start with penicillin –Garamycin - flagyl IVI.

Continue antibiotics for at least 14 days.

2. GIT

Pediatric surgeon must be consulted if there's perforation.

3. Cardio-respiratory

- Regular follow up by blood gases patient may need assisted ventilation.
- Plasma expanders or fresh blood or F.F.P.

4. Metabolic

NaHCO_3 to correct metabolic acidosis

5. Blood

Platelet conc. $\Rightarrow$ thrombocytopenia

Exchange transfusion may be needed.



Genetics

Patterns of inheritance

Single gene "Mendelian" Inheritance

- It describes those conditions where single mutant genes have a large effect on human health.
- Pedigree analysis is essential to determine the mode of inheritance of many traits.

Definitions

- Gene:** the hereditary factor that interacts with the environment to determine a trait.
- Alleles:** alternative forms of both normal and abnormal genes.
- Locus:-** is the physical location of the gene on a chromosome.
- Genotype:-** The genetic constitution of the individual.
- Phenotype:** The end result of both the genetic & environmental factors giving the clinical picture or the observed expression of the gene.
- Homozygous:-** The condition of having identical alleles at one locus; which can be either normal or abnormal.
- Heterozygous:-** The condition of having different alleles at one locus.
- Dominant condition:-** Evident in both homozygous & heterozygous.
- Recessive condition:-** Present only in homozygous state.
- Autosomal:-** It is gene is located on autosomal chromosome.
- Sex-linked:-** It is genes are located on (X) or / Y chromosome.
- Compound heterozygous:-** An individual with 2 mutant alleles (different) at one locus.
- Double heterozygous:-** an individual with 2 mutant alleles that are each at different locus.

Autosomal Dominant "AD"

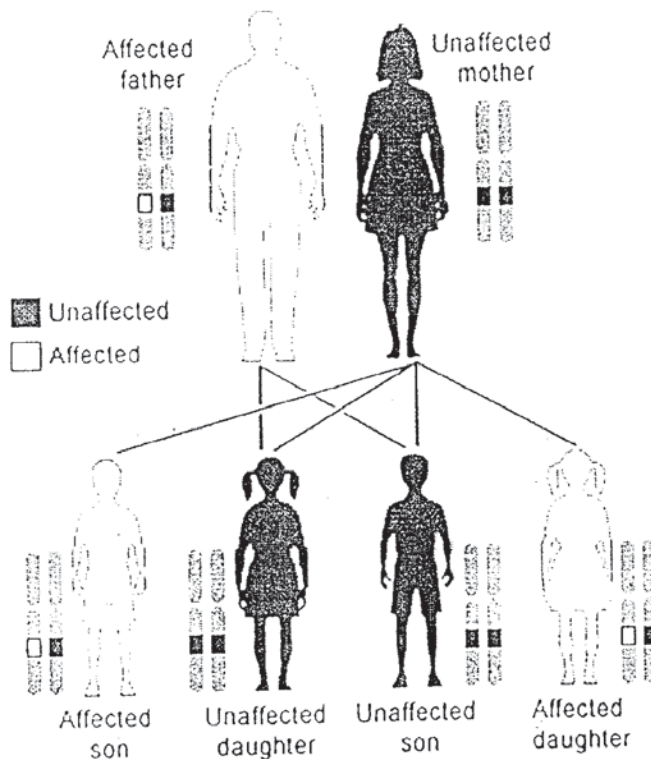
Characters

- One of the parents must be affected.
- The patient may be homozygous or heterozygous.
- Unaffected persons are phenotypically normal and genotypically normal.
- No sex difference.
- The parents might be clinically free in the following situations:
 - New mutation.
 - Variable expression of the gene.
 - Gene penetrance i.e. The disease might skip one or more generation e.g. disease in grandfather skip the father & reappear in his son.

Examples:

1. Achondroplasia.
2. Osteogenesis imperfecta tarda.
3. Osteopetrosis "Marble bone disease".
4. Spherocytosis & Elliptocytosis.
5. Neurofibromatosis and Huntington chorea.

Autosomal dominant



Autosomal Recessive "AR"

Character

1. Both parents are carriers or one is diseased & the other is carrier.
2. The affected person should be homozygous.
3. Unaffected persons (phenotypically normal) are either genotypically normal or are carriers (Heterozygous).
4. Consanguinity between parents is usually present.
5. Both sexes are equally affected.

Examples:

A-IEM:

1. Galactosemia
2. Phenylketonuria "PKU"
3. MSUD (maple syrup urine disease)

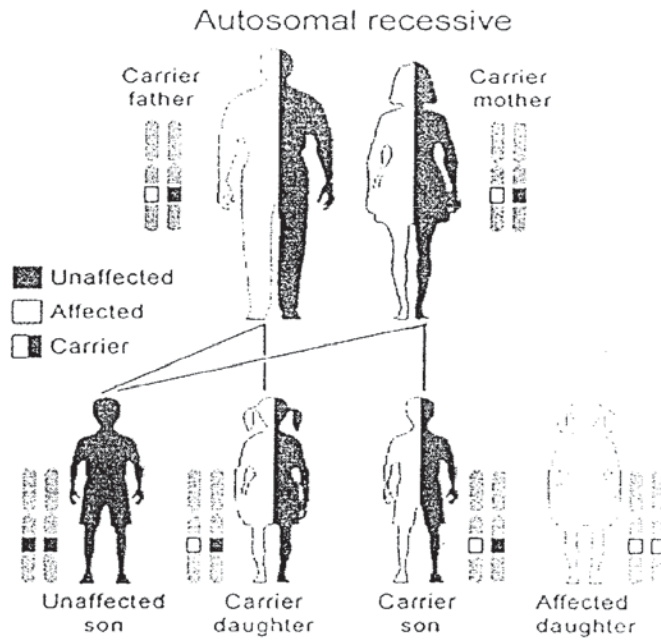
4. MPS.

B- Blood:

- 1- Thalassemia
- 2- Sickle cell

C. Neurological:

- 1- Friedreich ataxia

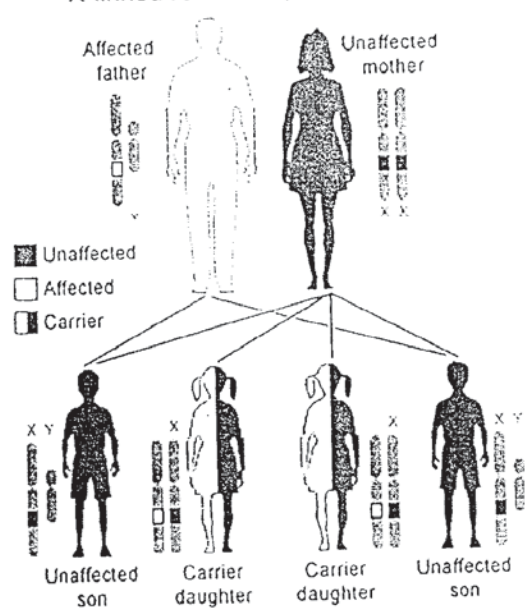


X-Linked Recessive "XLR"

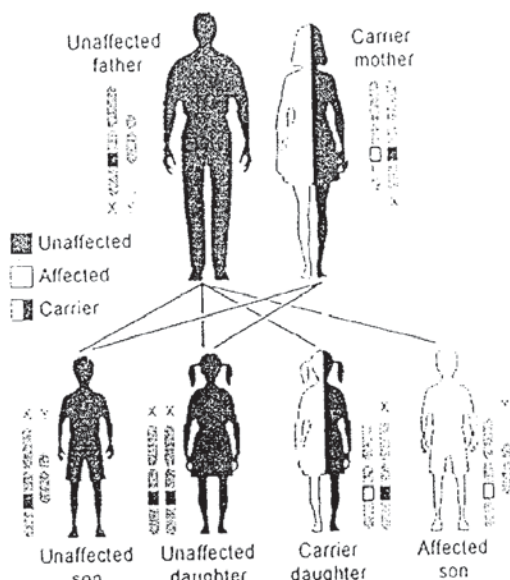
Characters

1. Common in males.
2. Affected father transmits the gene to all his daughters but never his sons.
3. A carrier mother will transmit the character to half of her sons "Diseased" & half of her daughters "carries".
- 4- Free mother = Free offspring.
- 5- Females are affected:
 - a. Diseased father & Carrier mother
 - b. Both parents are diseased
 - c. Turner "XO"
 - d. New mutation in a carrier female.
 - e. Lyon's theory in carrier female.

X-linked recessive, affected father



X-linked recessive, carrier mother



Examples:

A. Blood

Hemophilia A&B
G-6-PD deficiency

B. Neurological

Duchenne myopathy

X-Linked Dominant "XLD"

Characters:

1-Affected father

Females
All are
Diseased

Males
All are
Free

2-Affected mother "Homozygous"

Females
All are
Diseased

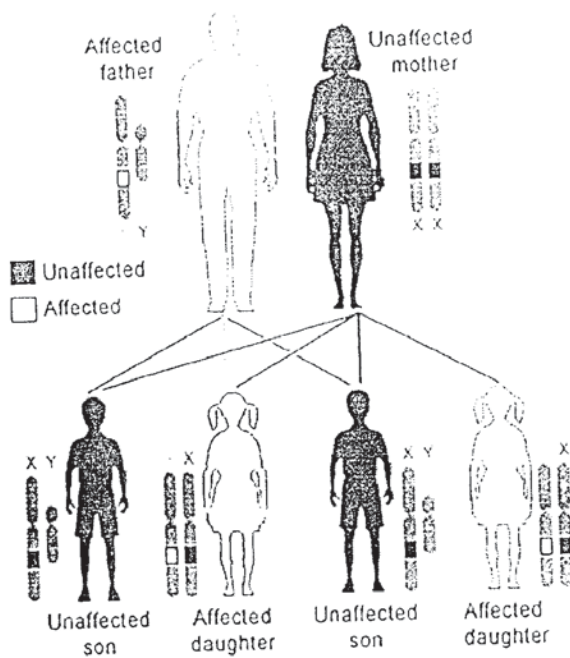
Males
All are
Diseased

3- The clinical Picture is more severe in females than males

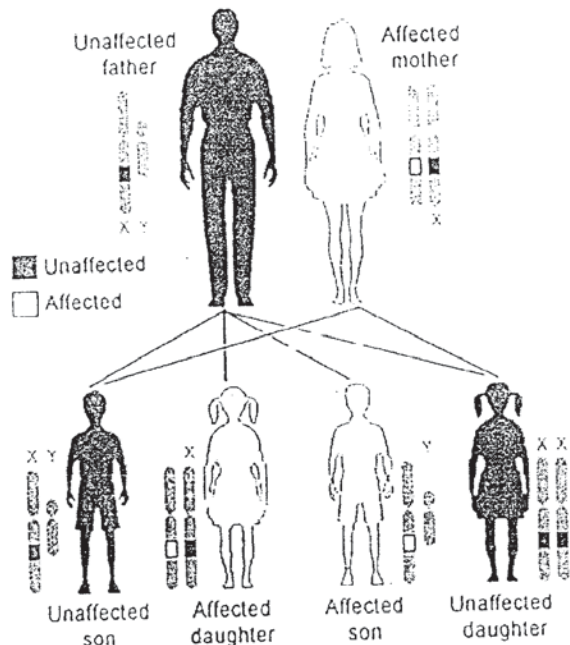
Examples:

Vit-D resistant rickets "1ry hypo - phosphatemic type"

X-linked dominant, affected father



X-linked dominant, affected mother



Y-Linked Inheritance "Hollanderic"

Characters:

- 1- Males are only affected.
- 2- Father transmit the gene to his Sons

Examples:

Hairy ear pinna

Germ-line mosaicism

In this condition parents are phenotypically normal by all known tests, but in which more than one of their offspring have been affected.

CO-dominance

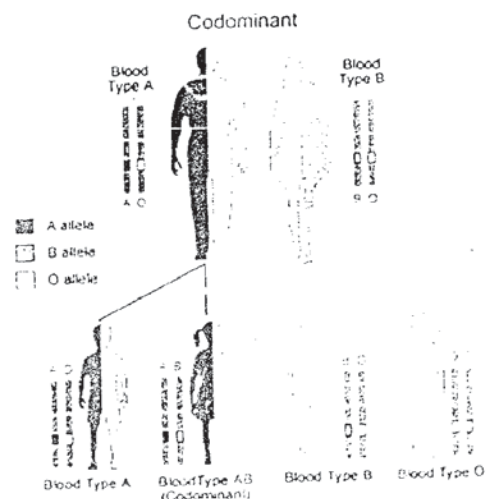
The two genes are dominant but not identical
e.g. ABO groups

Intermediate Inheritance

In which the heterozygote differs from individuals homozygous for the mutant allele.

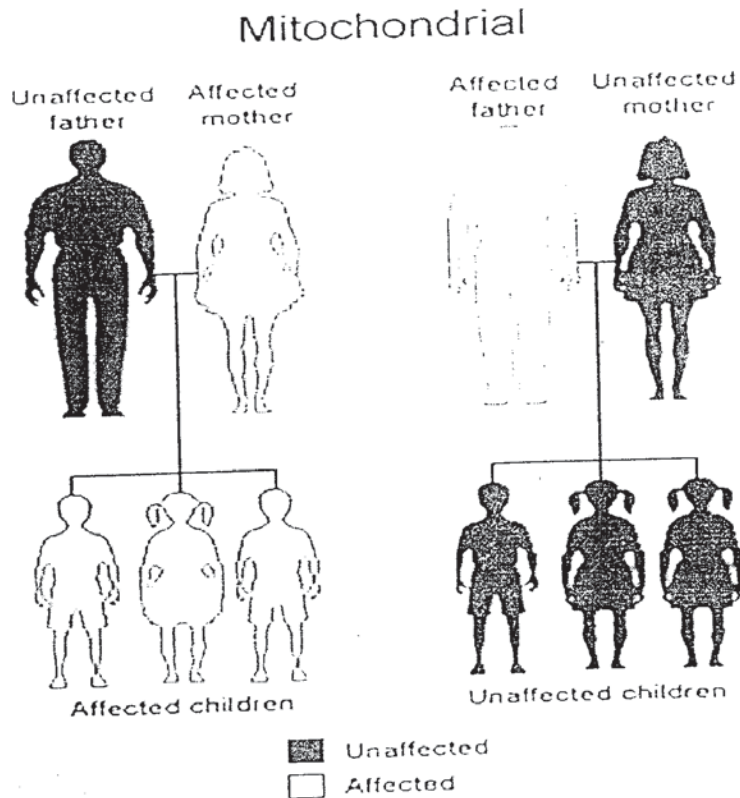
Genetic Heterogeneity

The same phenotype for different genotype.



Mitochondrial Inheritance

- Cells have hundreds of mitochondria dispersed throughout the cytoplasm, each containing a number of circular DNA are known to account for a small number of genetic conditions
- It is transmitted from mother to her offspring.



Multifactorial Inheritance

- These are traits that are due to the combination of many genetic (polygenic) and non-genetic factors. Genes and environmental factors affecting a given multi-factorial trait may vary among different individuals. Quantitative traits exhibit continuous variability.
- Qualitative traits follow multi-factorial threshold model, according to which all of an individual's genetic and environmental disease producing factors together, constitute liability which if exceeds a certain threshold the disease occurs.
- Some factors have to be considered in the multi-factorial inheritance model including ; sex, biological relation, consanguinity, concordance state and severity of the trait.
- Heritability is a measure of a proportion of the total variation in character (trait) attributable to genetic factors.

Sex-Chromatin

The human chromosomal structures are composed of 46 chromosomes (female is 46,XX & male is 46, XY).

Q: How to differentiate between male & female cells?

Barr body

If the cell contains more than one X-chromosome, the extra-chromosomes are found to form a deeply stained mass near the nucleus "Barr body"

Thus:

- | | | |
|-------------------------|---|------------------------------|
| 1. Normal male (XY) | ⇒ | Barr body -ve "chromatin-ve" |
| 2. Normal female (XX) | ⇒ | Barr body +ve |
| 3. Turner syndrome (XO) | ⇒ | Barr body -ve |
| 4. Klinefelter (XXY) | ⇒ | Barr body +ve |
| 5. Super-female (XXX) | ⇒ | 2 Barr bodies |

Drum-Stick

It's present in PMNL & corresponds to the barr body of other cells.
The extra-chromosome attains "Drum stick shape"

Fluorescent body

By using a special fluorescent dye the Y-chromosome. Can be stained & seen under the microscope.

Karyotyping

Will show the exact character of the chromosomes.

Chromosomal Aberration

Etiology

1. Old maternal age
2. Viral infections
3. Irradiations
4. Drugs
5. Certain genes may predispose to chromosomal aberrations. e.g. Gene for fragile X-chromosome predisposes to breaks in the chromosome X.
6. Some chromosomal aberrations predispose to another aberrations e.g. mother with BTC predisposes to translocation Mongol in her offspring.

Mechanisms

I- Non -disjunction

Failure of separation of the 2 homologous chromosomes or chromatids during the anaphase $\Rightarrow$ formation of 2-daughter cells

- One with extra-chromosome (24 chromosome).
- One with less-chromosome (22 chromosome)

II- Breakage

Apart of the chromosome is broken with the result of

1-Deletion

The broken part is lost

2- Translocation

The broken part is joined to another chromosome.

3- Inversion

The broken part is inverted & re-united to the same chromosome

4-Ring chromosome

The 2 terminal parts of chromosome are broken & the two terminal ends unite together forming a ring.

III. Iso- chromosome formation

Instead of longitudinal division of one chromosome to form 2 separate chromatids it divides at the centromere transversely to form 2 non-identical parts:

- One formed of 2 short arms
- One formed of 2 long arms

Each of them is called iso-chromosome

TYPES OF CHROMOSOMAL ABERRATION

- I. Numerical chromosomal aberrations
- II. Structural chromosomal aberrations

I. Numerical chromosomal aberrations

An-euploidy

- The number of chromosomes is not exactly the duplicate of 23.
- It's either 47 chromosome "Trisomy" or 45 chromosome "Monosomy".
- Monosomy is not compatible with life except in case of Turner syndrome "45,X"

Poly-ploidy

- The number of chromosomes is the multiple of 23 i.e. 3×23 , 4×23 ...etc.
- All these anomalies are incompatible with life & are usually found in abortions.
- Triploidy : is due to fertilization by 2 sperms.
- Tetraploidy : is due to failure to complete the 1st zygotic division.

Examples:

- 1- Trisomy of autosomal chromosomes
Trisomy 21, 18, 13
- 2- Trisomy of sex chromosomes
Klinefelter (XXY)
Super female (XXX)
Super male (XYY)
- 3- Monosomy of X-chromosome
Turner syndrome (XO).

B-Structural Chromosomal aberrations

I-Translocation.

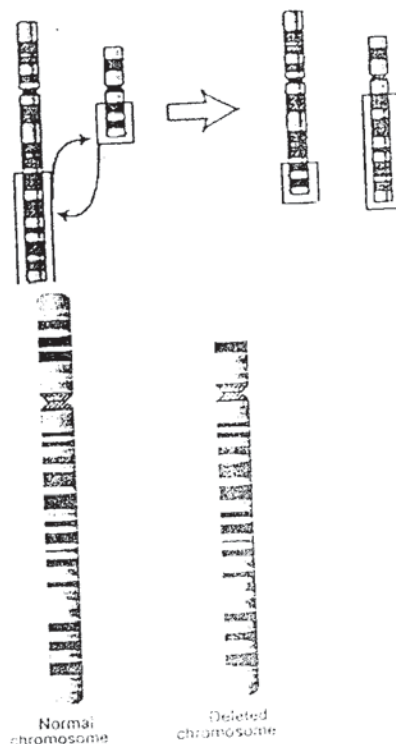
- A part of chromosome or the whole chromosome is translocated to another chromosome Balanced Translocation
Carrier "BTC"
- During gametogenesis, the faulty arrangement of chromosomes Unbalanced Translocation.

II- Deletion.

Simple breakage of one chromosomes with loss of small part of it

- e.g.
- 1- Cri-du-Chait syndrome (5p⁻)
 - 2- (4p⁻) syndrome
 - 3- Deletion of X-chromosome (Turner)

Translocation



Mongolism (Down syndrome)

Due to presence of an extra 21 chromosome

Incidence:

1/700 live births.

The incidence at conception is greater but more than 60 % are spontaneously aborted and at least 20 % are stillborn

Cytogenetic types:

I. Non-disjunction Mongol "95%"

- It's caused by failure of separation of the two chromosomes no.21 during meiosis $\Rightarrow$ formation of an ovum containing an extra-21 chromosome.
- It's an age dependent type, the older the maternal age, the more common the incidence.
- The Karyotyping of the baby is 47 with an extra-21 chromosome
- The mother has a normal Karyotyping 46
- It's the most common type "95%"
- The risk increases with age, about 1 in 200 for a 36 years old mother rising to 1 in 100 at 39 years and 1 in 50 at 42 years.

II. Translocation Mongol "4%"

In this type the extra 21 chromosome is translocated to another chromosomes:-

- To chromosome 14 (the most common).
- To chromosome 15
- To chromosome 13
- To chromosome 22
- To chromosome 21 $\Rightarrow$ the most serious prognosis why?

The mother

Is a BTC, with a Karyotyping of 45 chromosome + translocation of 21 chromosome to another chromosome. While the Mongol is 46 chromosome + translocation

Theoretically

The recurrence risk in case of translocation of 21 to 13,14,15,22 is $\frac{1}{3}$ of the living births.

However

The true recurrence risk is about 10-15 % "if the mother is a BTC" while 2% if the father is a BTCwhy?

In case of translocation 21 to 21 the risk is 100 % (the worst prognosis)

III. Mosaic Mongol: (1 %)

See before (mentality is less affected).

CLINICAL PICTURE

I. Mental deficiency

Presenting as delayed milestones of development

II. Growth retardation

Presenting as delayed growth "wt & height"

III. Characteristic physical signs

A. Head manifestations:

Delayed closure of The anterior fontanel & fine silky hair

- Depressed Nasal bridge.
- Brachy cephal.
- Medial epicanthic fold.
- Narrow palpebral fissure.
- Upward slanting Eyes.
- Apparent squint.
- Brush field iris.
- Retro-micrognathia.
- Delayed Eruption of teeth & small oral cavity
- Scrotal tongue (protruded fissured tongue).

B. Limb manifestations:-

- Inclino-dactyly (the little finger is incurved inward & has single crease due to rudimentary middle phalanx)
- Brachydactyly (short fingers)
- Single crease in the palmar aspect (simian crease) complete or partial
- Big space between 1st & 2nd toes

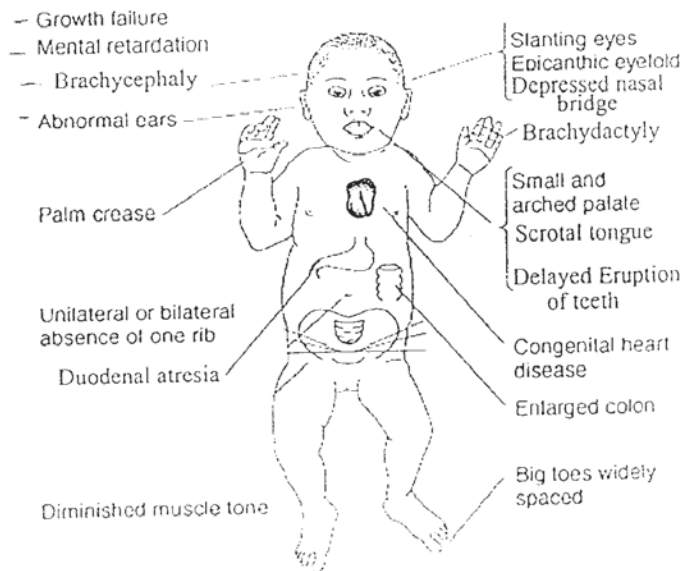


IV. Hypotonia:

- Marked laxity of the ligaments (Acrobatic sign).
- Viscero-ptosis.
- Pot-belly abdomen.
- Umbilical hernia.

V. Auto-immune diseases

- Hashimoto thyroiditis



9 down - related autosomes
 ① autosomes
 ② chromosomes

Management

a. Genetic counseling

- 1- A mother who is over 35 years ,with normal children then gets a Mongol $\Rightarrow$ mostly non-disjunction
So the possibility to get another Mongol is Low but still higher than younger mother
- 2- A young mother who gets a Mongol with history of repeated abortions $\Rightarrow$ mostly the mother is BTC

Do Karyotyping

21 Translocation to

14,13,15,22

1/3 of live-born
 will be Mongol

21 Translocation to 21

100% of living
 children will be Mongol

So:

Amniocentesis & Karyotyping of the amniotic fluid is indicated in

- ① Pregnant women over 35 years
- ② Mothers known to be BTC
- ③ Mothers with a history of birth of a Mongol.

Treatment

There's no specific curative treatment the aim is

1. Treatment of associated congenital anomalies & infections.
2. General nutritional, hygienic & medical care.
3. Special social, educational & behavioral therapy in specialized institute.

Anti-mongolism

It's caused by deletion of long arm of chromosome 21

CLINICAL PICTURE

1. MR
2. Growth retardation
3. Microcephaly
4. Congenital anomalies as

- Hypospedius & cryptorchidism
- Pyloric stenosis & inguinal hernia
- Micrognathia & high arched palate.
- Skeletal & nail anomalies.

general
 MR
 GR
 microcephaly



$\rightarrow$ downward slanting eyes
 $\rightarrow$ Brush

In contrast to Mongol there are

- i. Hypertonia.
- ii. Downward slating eyes. *and to show*
- iii. Prominent nasal Bridge.
- iv. Big ears.

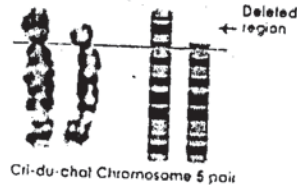
Hypertonia
125

Cri-du-chat syndrome

Due to deletion of short arm of chromosome no.5 (5P-)

CLINICAL PICTURE

- MR
- Growth retardation
- Microcephaly
- Congenital heart disease
- Marked hypertelorism
- Cat-like cry due to laryngeal hypoplasia
- Rounded face.



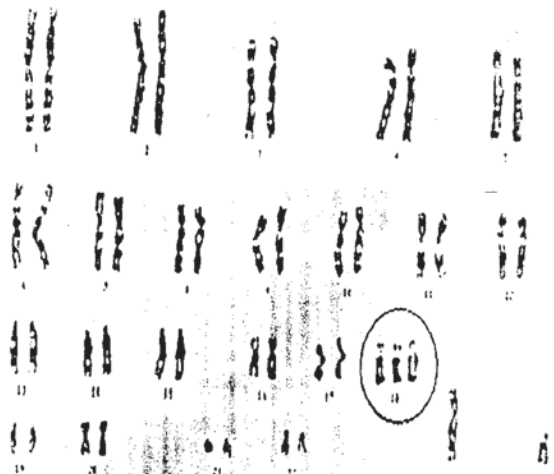
Trisomy 18 "T18" Edward's

Incidence

1 / 3000 live births
Male / Female ratio = 1/3 because there is increase spontaneous abortion in male fetus

CLINICAL PICTURE

- MR
- Growth Retardation
- Microcephaly
- Congenital heart disease
- Micrognathia
- Short sternum & narrow pelvis
- Hernias: inguinal & umbilical.



Characteristic features:

- ① Hypertonia.
- ② Prominent occiput.
- ③ Low set (malformed) ears.
- ④ Clinched fist.
- ⑤ Rocker bottom heel.



Down syndrome
phenotype
Down syndrome

Death frequently in early infancy or early childhood due to multiple congenital anomalies or pneumonia (only 10 % survive beyond 1st year).

Treatment

- 1- General supportive care
- 2- Genetic counseling.

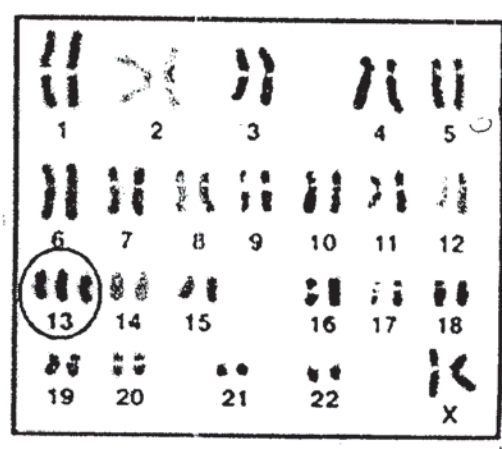
Trisomy 13

Incidence

1/ 5000 of live births

Clinical Picture

- MR
- Growth retardation
- Microcephaly
- Congenital heart disease "VSD"
- Midline facial defects :
 - Absent nose
 - Single nostril (cebocephaly).
 - Single eye (cyclopia).
 - Microphthalmia
 - Cataract
 - Anophthalmia
 - Coloboma.
 - Cleft lip / palate
- Polydactyly
- Low set ears
- Umbilical hernia
- Cryptorchidism
- Rocker bottom heels
- Capillary hemangiomas



Down syndrome
phenotype
Down syndrome
Speech
midline

Treatment

- 1- supportive care

meningitis
in Down syndrome

Turner Syndrome "45,XO"

Incidence

1 / 5000 of living female newborns

Spontaneous abortion occurs in 95% of affected pregnancies & only 5% are born alive.

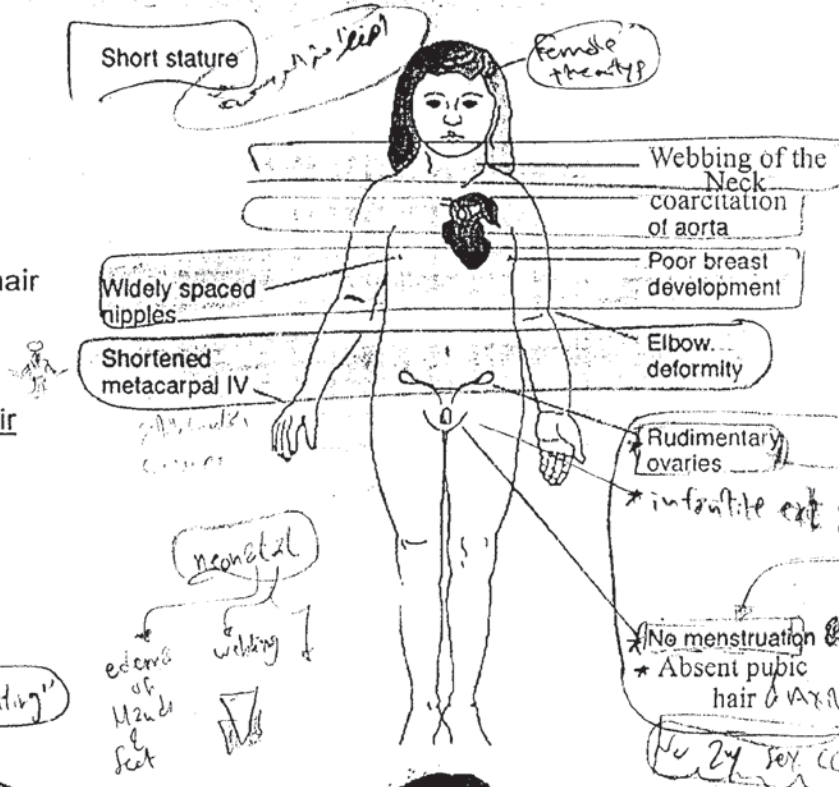
Clinical Picture

Female phenotype.

- Short stature
- Webbing of the neck
- Coarctation of the aorta
- Widely spaced nipple.
- Absent or minimal axillary hair
- Breast is not developed
- Cubitus valgus
- Wide carrying angle
- Absent or minimal pubic hair
- Infantile external genitalia
- 1st amenorrhea & sterility
- Streaked atrophic gonads

In the neonatal period

- ❖ Webbing of the neck
- ❖ Triangular face
- ❖ Coarctation of aorta
- ❖ Edema of hands & feet "new pitting"



Widely spaced nipple in Turner

Investigations

if > 16 yrs
اذا > 16 سنة

- ① ↑↑ Serum pituitary gonadotropins, FSH & LH. *No -ve Feed Back*
- ② ↓↓↓ Serum level of female sex hormones esp. Estrogens
- ③ Buccal smear ⇒ *NO* Barr body.
- ④ Karyotyping

May show one of the following

- Monosomy -X (45,XO) (common) ← classic
- Mosaicism 45,XO / 46,XX → Buccal smear - Barr Body +ve
- Iso-chromosome of the long arm of one X-chromosome (2 long arms with no short arms)

45,XO is the most common karyotype in Turner syndrome. Fertility is usually absent. Mosaicism is seen in about 10-15% of cases.

Deletion of short arm

Short stature

Turner phenotype

But no ovarian dysfunction

Deletion of long arm

Failure of ovarian development.

⇒ 46,XXp-

Treatment

GH then Estrogen replacement therapy

- 1- Help development of 2nd sexual character
- 2- Permit normal menses
- 3- Prevent development of osteoporosis



During pregnancy Turner syndrome may present with generalized edema (Hydrops) or localized nuchal swelling which may be mistaken on ultrasonography as encephalocele. This is due to delayed maturation of the lymphatic system.

- ① normal
 - ② deletion of short arm
 - ③ isochromosome of long arm
 - ④ mosaicism 45,XO / 46,XX
- on VUS scan

Klinefelter Syndrome (47,XXY)

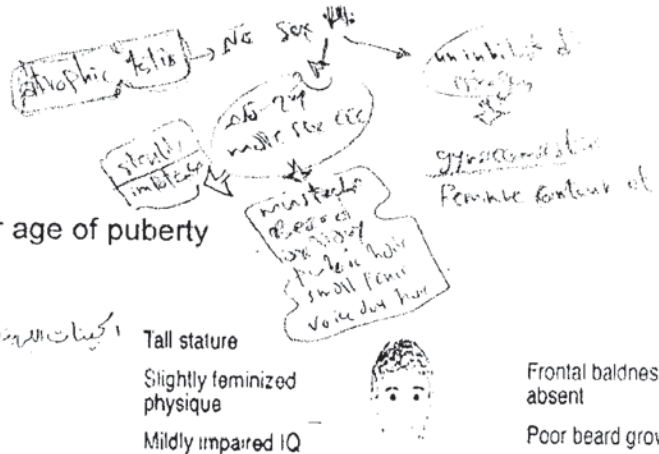
Incidence

- 1/1000 of living newborn males
- It's associated with old maternal age.

Clinical Picture

Characteristic Feature do not appear- till after age of puberty

- Male phenotype
- Tall stature due to marked delay in epiphyseal closure (Androgens) + (b) *delayed epiphyseal closure*
- Gynecomastia & feminine contour of the body
- Small atrophic testes
- Failure of 2ry sexual characters to develop e.g. mustache, beard, axillary & pubic hairs in addition to small penis . The voice does not become harsh.
- Sterility & Impotence with lack of libido
- Mentality may be affected, especially with more than 2 X chromosomes.



Investigations

1. ↑↑↑Pituitary gonadotropins (LH & FSH)
2. ↓↓↓Male sex hormones (testosterone) "*delayed testis*"
3. Buccal smear ⇒ Barr body +ve
4. Testicular biopsy ⇒ Hyalinization & atrophy
5. Karyotyping may show one of the following
 - a. 47,XXY in the majority of patients
 - b. Rare variants ⇒ 48,XXY, 49,XXXX
 - c. Mosaics ⇒ 46,XY & 47,XXY (some)

Treatment

Testosterone replacement therapy → *male 2ry sex char*

Super-male (47XYY)

- This syndrome presents in 10% of tall men (*taller than 180 cm*) with defective aggressive personality, which may lead to conflicts with law
 - Abnormal behavioral pattern is usually present since childhood.
- Mentality ⇒ may be slightly affected.
Fertility ⇒ may be normal

Fragile -X Syndrome

- It account for more than 30- 50 % of cases of X-linked mental deficiency in males & 10% of cases of MR in females
- It's caused by spontaneous breaks of the long arm of X- chromosome.
- This syndrome is inherited in an X-linked recessive manner.

Clinical Picture

1. MR: more severe in males
2. Oblong face with large ears & prominent jaw
3. Markedly big testes in affected males esp. after puberty with normal size of penis.
4. In childhood, autism & convulsions may occur.

Investigations

Karyotyping Using a special technique, the fragile part at the end of long arm of X- chromosome can be demonstrated.

Super-female (47,XXX)

Clinical Picture

1. (MR) more severe with more X-chromosome.
2. Tall stature.
3. All her children will be normal.

Thinking of
Down

O: What are the indications of Karyotyping?

Indications of Karyotyping

- ① Confirmation of suspected diagnosis of chromosomal etiology.
- ② Persons with multiple congenital anomalies.
- ③ Mothers of repeated spontaneous abortion
- ④ Female with 1^{ry} amenorrhea or sterility
- ⑤ Abnormal external genitalia
- ⑥ All persons with MR of unknown cause.
- ⑦ Ambiguous genitalia
- ⑧ Female with short stature of unknown etiology
- ⑨ Pregnant mother over 35 years.
- ⑩ Mothers with BTC
- ⑪ History of previous child with chromosomal abnormality.

Triple test

Screening (20) (20, 1, 0)

1. Adaptation

18. *Chlorophyll* *chlorophyll*

A. A. ...

From the above it follows that

[illegible]
$$148000 - (50000) =$$

Q: calculate chemical shift $\rightarrow$ MR Solids (mg) $\neq$ then

(A) 2.514/100 = 1/4000

5.

$\Delta \xrightarrow{\text{frag.}} \gamma$ clear

superficial

Information [Slight error]

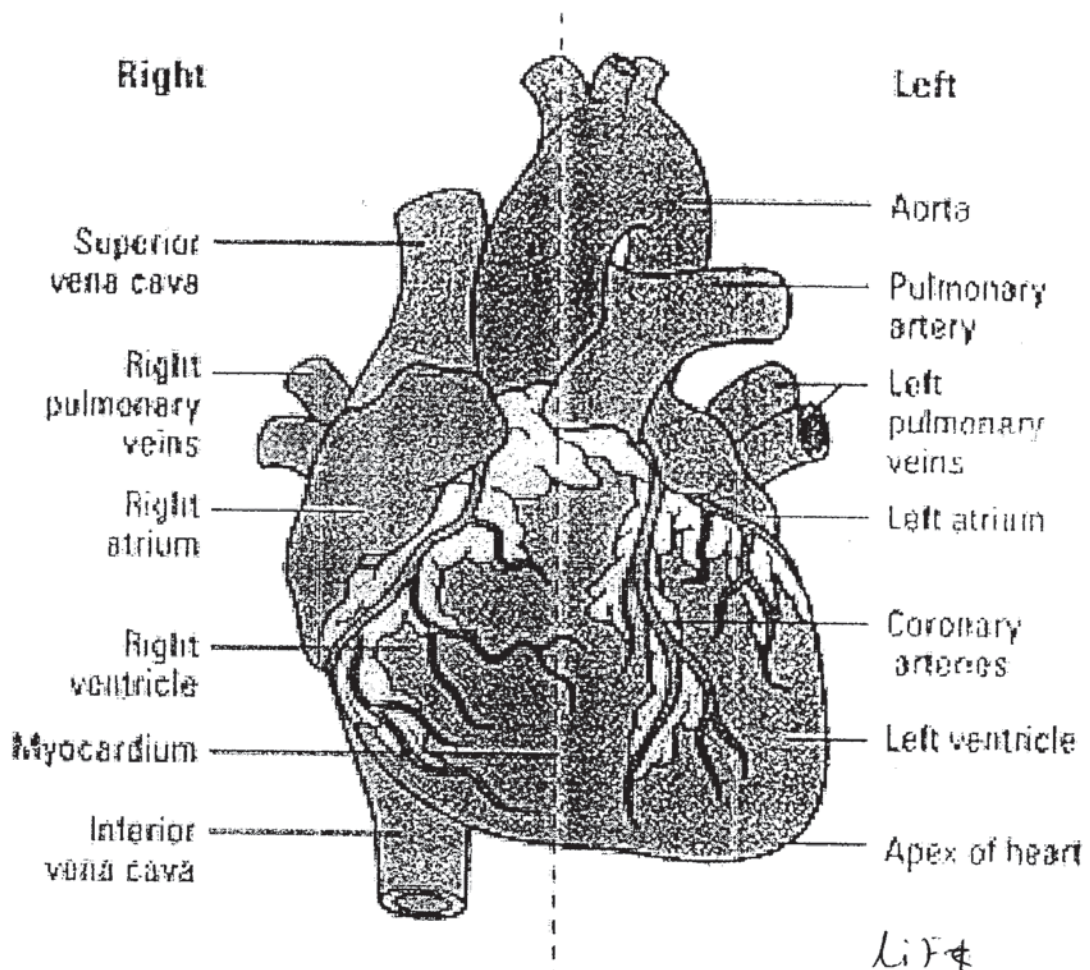
Leptis de la m. ing. 2000

[illegible]


 Left side breakage design up
 X change more

1000

The Heart: Outside



Apex → 7275cm,
77 → 27cm
775cm

Left
Fourth space outside midline
out
Fifth ~ ~ ~

Cardiology

Congenital Heart Diseases

Incidence

- It is the commonest congenital anomalies 30 %.
- This equal 8/ 1000 live births.
- The commonest are VSD, PDA & ASD.

Etiology

- Multifactorial inheritance means that abnormalities of the gene concerned with heart development (+ve family history) on the presence of other environmental factors lead to heart defects, if the environmental hazards occur during 2-9 weeks of pregnancy. *Conid*
 - The most common cause is idiopathic.
 - Congenital infections e.g. congenital rubella syndrome.
 - Teratogenic effect of drugs e.g. aspirin, lithium, warfarin or irradiation.
 - Associated with chromosomal disorders. Down, Marfan, Turner & Noonan syndromes.
 - Associated with some maternal diseases as DM, PKU, SLE.

Classification

- CHD are classified into acyanotic & cyanotic HD.

Acyanotic	Cyanotic
A. Shunts - VSD - ASD - PDA	A. With oligemic lung - Fallot's tetralogy - Tricusped atresia
B. Obstructive - Aortic stenosis - Pulmonary stenosis	B. With plethoric lung - Transposition of great vessels - Truncus arteriosus
C. Malposition Dextrocardia	

- All cases with Lt to Rt shunt are considered potentially cyanotic.

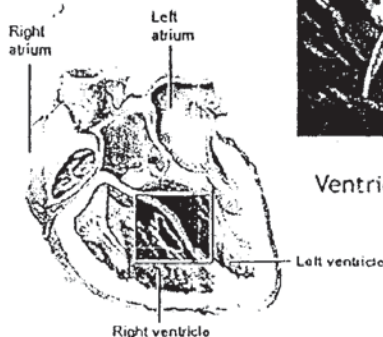
Ventricular Septal Defect (VSD)

Definition

- It is defect in the interventricular sept

Etiology

- Idiopathic type.
- congenital infection: e.g. congenital rubella syndrome
- Teratogenic factors: e.g. drugs during pregnancy as aspirin
- Chromosomal: e.g. Down's syndrome.



Ventricular septal defect

Types

A. According to the site:

1. Upper $\Rightarrow$ Membranous
2. Lower $\Rightarrow$ Muscular

B. According to the Size:

1. Small: $< 0.5\text{cm}$
2. Average: $0.5 - 1\text{cm}$
3. Large: $> 1\text{cm}$

Hemodynamics

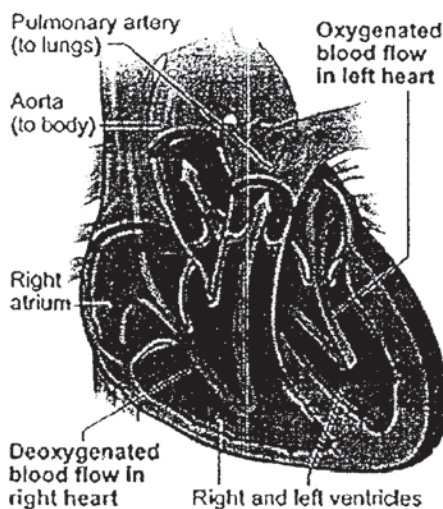
1. Small defect:

- No significant changes & pulmonary hypertension does not occur.
- 75 % will have closure of the defect by 10 years of age (Roger's disease)

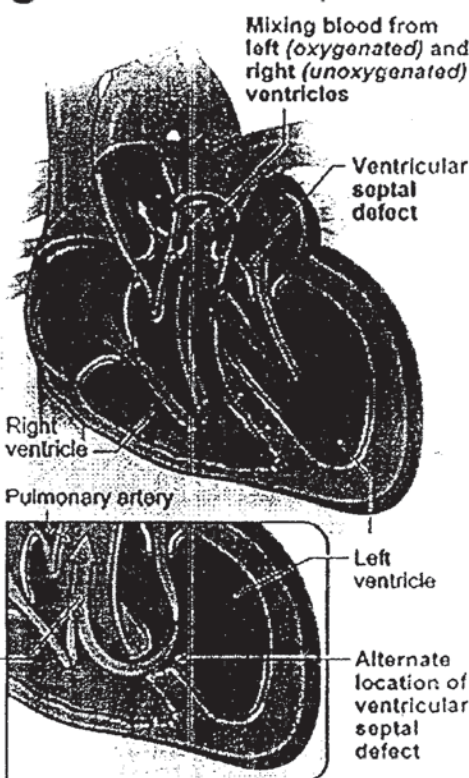
2. Large defects:

- The blood From the Lt ventricle is divided into 2 portions one part passes to the aorta and the other one passes to the Rt ventricle $\Rightarrow$ RV++.
- All this blood will pass through the pulmonary artery $\Rightarrow$ Pulmonary plethora $\Rightarrow$ Symptoms of pulmonary congestion.
- Then, pass to the Lt atrium $\Rightarrow$ Lt atrium dilatation.
- Then, to the Lt ventricle $\Rightarrow$ LV dilatation.
- Persistent of pulmonary plethora $\Rightarrow$ P++ $\Rightarrow$ Low COP symptoms.
- Pulmonary hypertension $\Rightarrow$ $\uparrow\uparrow\uparrow$ Rt ventricular pressure $\Rightarrow$ Eisenmenger Syndrome $\Rightarrow$ Persistent cyanosis

A Normal heart



B Hearts with ventricular septal defects



Down $\Rightarrow$ Common AV canal
Tricuspid $\Rightarrow$ Midline defects.
Turner $\Rightarrow$ Coarctation of aorta
Marfan $\Rightarrow$ C. aorta incompetence.
Neonatal $\Rightarrow$ C. Pulmonary stenosis
Turner $\Rightarrow$ A. arch anomaly.
Alagani $\Rightarrow$ P. stenosis.

Clinical Picture

Symptoms:

1. Asymptomatic: this is the usual presentation in small VSD which is accidentally discovered during routine examination of the heart.
2. Congestive lung symptoms.
3. Palpitation. *→ the case of murmur but very obvious*
4. Low COP symptoms: when he developed pulmonary hypertension.
5. Potential cyanosis: especially on crying due to $\uparrow\uparrow$ pulmonary pressure $\Rightarrow$ transient reversal of the shunt.
6. Permanent cyanosis: when he developed Eisenminger syndrome.

Signs:

A. Inspection & palpation:

1. Pericardial bulge: in long standing cases.
2. Apex:
 - Site: shifted downward & outward.
 - Size: diffuse.
 - Character: hyper dynamic.
 - Thrill: systolic maximum on the Lt parasternal area.
3. Parasternal pulsations.
4. Epigastric pulsations.
5. Diastolic shock over the pulmonary area in cases complicated by P⁺⁺

B. Percussion: dullness over the pulmonary area in cases complicated by P⁺⁺.

C. Auscultation:

- ❖ S1: normal.
- ❖ S2: $\uparrow\uparrow\uparrow$ in cases complicated by P⁺⁺.
- ❖ Murmur:
 - Timing: Pan systolic.
 - Character: Harsh.
 - Site of maximum intensity: Lt 3rd & 4th parasternal area.
 - Propagation: all over the pericardium.

Complications

1. Repeated chest infections.
2. Infective endocarditis
3. Congestive HF.
4. Eisenminger syndrome $\Rightarrow$ reversal of the shunt due to development of P⁺⁺ $\Rightarrow$ permanent cyanosis & clubbing of the nails.
5. Stunted growth.

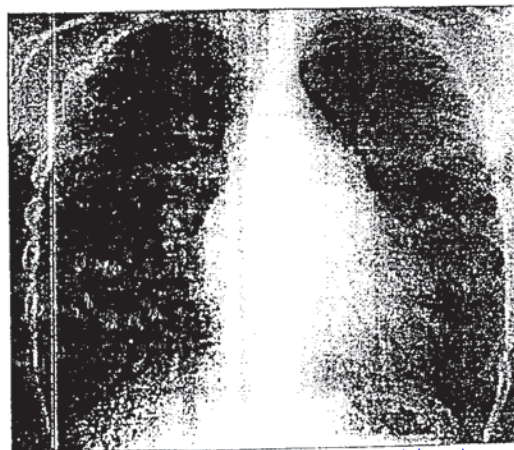
Investigations

1. CXR

All chambers of the heart are enlarged except the Rt atrium.

- Large pulmonary arteries
- Pulmonary plethora.

2. ECG $\Rightarrow$ Evidence of Bi-ventricular hypertrophy and Lt atrial dilatation
 - P- Pulmonale with the development of P⁺⁺



3. Echo - Cardiography

Can demonstrate the site, size & direction of flow through the shunt.

4. Cardiac catheterization.

Treatment

A. Medical TTT:

Prophylaxis against infective endocarditis.

B. Surgical TTT: It is indicated in:

1. Membranous VSD regardless the size.
2. Large muscular VSD.
3. Increasing pulmonary artery pressure.
4. If still present after the age of 5 years.

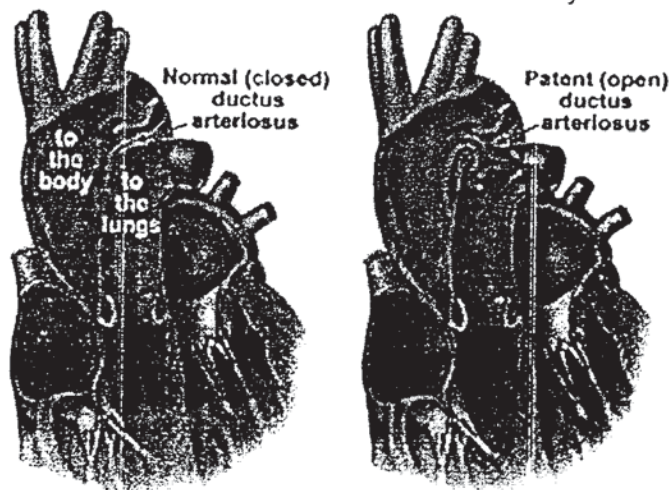
Roger's disease $\Rightarrow$ small VSD in the muscular part of the septum. There's no hemodynamic disturbance.

- Usually accidentally discovered
- O/E $\Rightarrow$ Harsh loud ejection systolic murmur maximum over the 3rd & 4th Lt parasternal area
- Spontaneous Closure is the rule

PDA

Definition

It is persistence of the fetal communication between the main pulmonary artery & the aortic arch after the origin of the Lt subclavian artery.



Mechanism of closure

1. Functional closure

- At birth $\Rightarrow$ blood passes from the aorta to the pulmonary through DA, this blood is oxygenated $\Rightarrow$ stimulation of local axon reflex $\Rightarrow$ inhibition of PGE2 release from the endothelial cells of DA $\Rightarrow$ contraction of the wall of the ductus 'This occurs within 10-15 hrs of birth'

2. Later, clots form $\Rightarrow$ fibrosis $\Rightarrow$ obliterative closure.

Spontaneous closure may occur up to 3 months after birth of premature.

From Above

1. Maternal PGE2 $\Rightarrow$ PDA
2. Neonatal anoxia $\Rightarrow$ PDA
3. Anti - prostaglandins $\Rightarrow$ closure of the ductus
4. Congenital rubella $\Rightarrow$ Proliferation of endothelial
 $\Rightarrow \uparrow$ PGE2 $\Rightarrow$ PDA

Hemodynamics

1. The pulmonary receives blood from the aorta &
RV $\Rightarrow$ Lung plethora $\Rightarrow$ LA++ $\Rightarrow$ LV ++
2. After sometime $\Rightarrow$ P ++ occur $\Rightarrow$ Reversal of the shunt
 $\Rightarrow$ Eisenminger syndrome $\Rightarrow$ Persistent cyanosis in
the lower half of the body "Differential Cyanosis"

Clinical PictureSymptoms:

1. Asymptomatic: This is the usual presentation in small PDA.
2. Congestive lung symptoms.
3. Palpitation.
4. Low COP symptoms: in the lower limbs only.
5. Differential cyanosis in the lower limbs only: when he developed Eisenminger syndrome.

Signs:

- General signs:
 - 1) Water hammer pulse.
 - 2) Cyanosis & clubbing in both lower limbs when he developed Eisenminger syndrome
- Local signs:
 - 1) Inspection & palpation:
 - Apex:
 - Site: shifted downward & outward.
 - Size: localized
 - Character: hyper dynamic.
 - No parasternal pulsations.
 - No epigastric pulsations.
 - Diastolic shock over the pulmonary area in cases complicated by P++.
 - Thrill: can be felt below the left infra-clavicular area.
 - 2) Percussion:
 - Dullness over the pulmonary area in cases complicated by P++.
 - 3) Auscultation:
 - S1: normal.
 - S2: in cases complicated by P++
 - Murmur:
 - Timing: continues.
 - Character: machinery.
 - Site of maximum intensity: below the left clavicle.
 - Propagation: to the pulmonary area & back.

Complications

1. Repeated chest infections.
2. Infective endocarditis.
3. Congestive HF.
4. **Eisenminger syndrome** $\Rightarrow$ reversal of the shunt due to development of $P^{++} \Rightarrow$ permanent cyanosis & clubbing of both lower limbs.
5. Stunted growth mainly in the lower segment.

Investigations

1. CXR

- All chambers of the left side of heart are enlarged.
- Large pulmonary arteries
- Pulmonary plethora.

2. ECG

- Evidence of Lt-ventricular and Lt atrial dilatation
- P- Pulmonale with the development of P^{++} .

3. Echo-Cardiography

- Can demonstrate the size & direction of flow through the shunt.

4. Cardiac catheterization

Treatment

A. Medical:

- Prophylaxis against infective endocarditis.
- If the condition diagnosed early anti-prostaglandin as Indomethacin can be given.

B. Surgical TTT: It is indicated as soon as possible

ASD

Definition

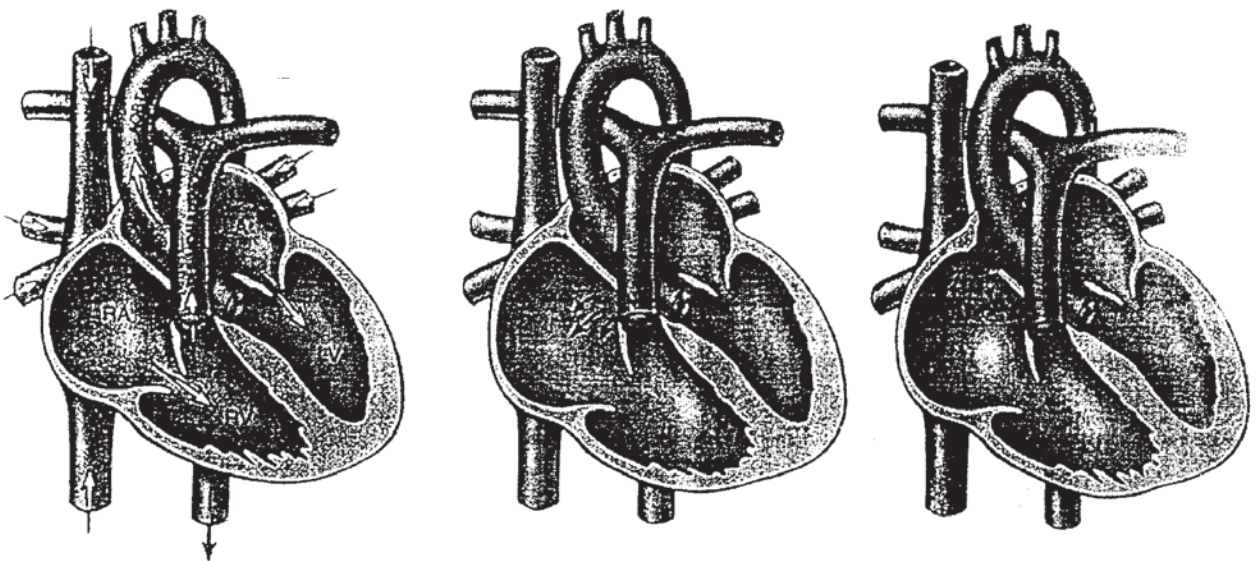
- It is defect in the inter-atrial septum

Etiology

- As VSD

Types

1. Ostium primum $\Rightarrow$ defect in the lower part of the septum "less common"
2. Ostium secundum $\Rightarrow$ defect in the upper part of the septum "more common"
3. Patent foramen ovale
4. Endocardial Cushion defect "common A-V canal" Ostium primum defect + High VSD + TI $\pm$ MI
the common congenital heart disease in Down's syndrome



Hemodynamics

1. Lt atrial pressure is more than the Rt atrium So part of blood is shunted from LA to RA which receives blood from the superior & inferior vena-cava $\Rightarrow$ RA ++.
2. This big amount of blood goes to the RV $\Rightarrow$ RV++ $\Rightarrow$ to the pulmonary A. $\Rightarrow$ enlargement of the pulmonary artery, $\Rightarrow$ lung plethora $\Rightarrow$ repeated chest infection.
3. Then to LA where part of blood is shunted to RA & the rest goes to LV $\Rightarrow$ Aorta.

C/P

1. Small defect usually asymptomatic
2. Dyspnea & recurrent chest infection "due to pulmonary plethora".
3. Growth retardation
4. O/E
 - Rt ventricular enlargement.
 - Wide, Fixed splitting of the 2nd heart sound on the pulmonary area.

N.B. Passage of blood through the ASD produces no murmurs. But, soft ejection systolic murmur may be heard over the pulmonary area due to function P.S.

Investigations

1. CXR:

- All Chambers of the heart are enlarged except the LV
- Large pulmonary arteries & plethora.

2. ECG:

- RV⁺⁺
- Rt bundle branch block (RBBB)

2. Echo-cardiology & cardiac catheterization ⇒ diagnostic

Complications

1. Recurrent chest infections.
2. H.F. "Rt. ventricular"
3. Infective endocarditis is rare due to low pressure gradient.
4. Eisenmenger syndrome " uncommon & late"
5. Lutembacher syndrome ⇒ ASD + rheumatic Ms.

Treatment

Surgical closure of large defects

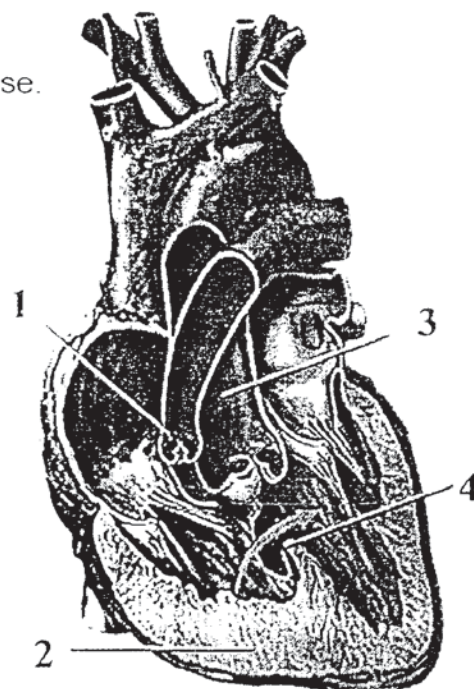
Fallot's tetralogy

Definition

- It is the most common congenital cyanotic heart disease.
- It consists of tetrad
 1. Infundibular "subvalvular" PS
 2. RV hypertrophy
 3. Over-riding aorta
 4. Big membranous VSD.

Hemodynamics

- The blood in the RV will pass through 2 ways.
- 1. Small amount passes through the narrow pulmonary to the lung ⇒ lung oligemia. This small amount will be oxygenated & pass to LA ⇒ LV ⇒ aorta.
- 2. Larger amount will pass non oxygenated to the overriding aorta ⇒ cyanosis.
- The RV enlarges but not markedly because the blood has 2 ways to leave.



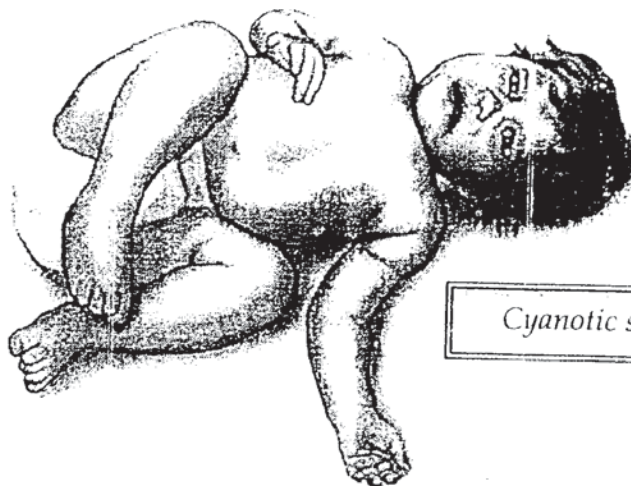
Clinical Picture

1. Central Cyanosis: appearing shortly after birth --- why?
2. Clubbing of fingers ⇒ usually drum stick.
3. Squatting position: Preferred by the patient because.
 - a. Kinking of femoral & popliteal arteries ⇒ ↑↑ resistance to blood going through the aorta & so forces more blood to pass to the lungs.
 - b. Blood is squeezed from L.L. & splanchnic area, so more blood goes to the brain.



4. Cyanotic spells

Due to spasm of the infundibulum forcing all blood in RV to the aorta
 unoxygenated $\Rightarrow$ cerebral hypoxia $\Rightarrow$ syncope & cyanosis became more deep $\Rightarrow$
 convulsions.

5. Stunted growth

Cyanotic spell

O/E

1. No pulsation or dullness over the pulmonary area.
2. The 2nd sound over the pulmonary area is:
 - a. Single: aortic component only.
 - b. Accentuated: due to $\uparrow\uparrow$ aortic blood flow:
3. Harsh ejection systolic murmur maximum over the pulmonary area "PS".
 - a. Inversely proportionate to severity of PS
 - b. It is $\Rightarrow$ uncommonly accompanied with thrill.

Complications

1. Cyanotic spells
2. Pulmonary T.B.
3. Polycythemia $\Rightarrow$ $\uparrow\uparrow$ thrombosis.
4. Cerebral thrombosis.
5. Brain abscess $\rightarrow$ why?
6. Infective endocarditis & HF are rare.
7. Growth retardation & delayed puberty.

Investigations1. CXRa. Coeur en sabot:

- Enlarged aorta.
- Small pulmonary artery (exaggerated waist).
- RV enlargement.

b. Oligemic lung fields.2. ECG $\Rightarrow$ slight RV hypertrophy.3. Echo-cardiography & cardiac catheterization.

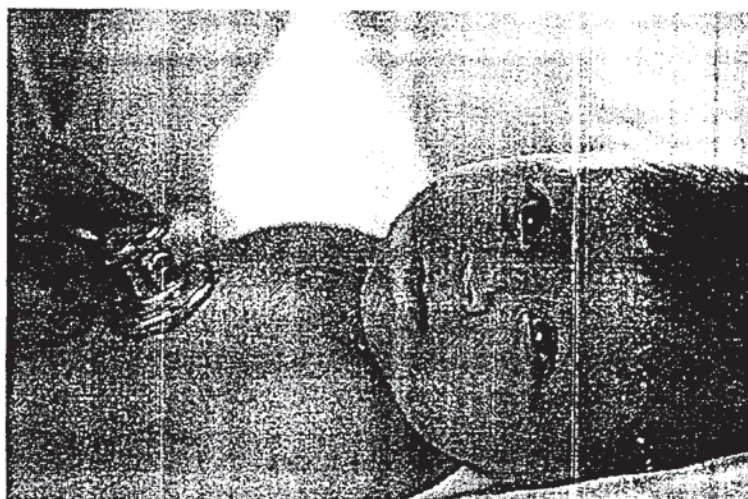
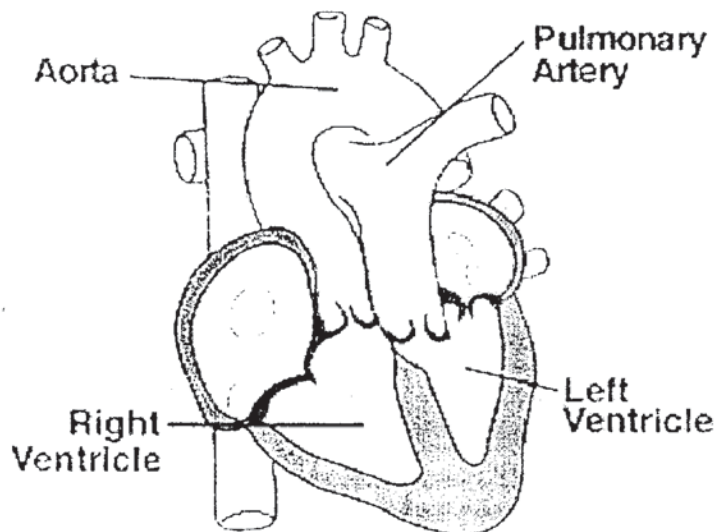
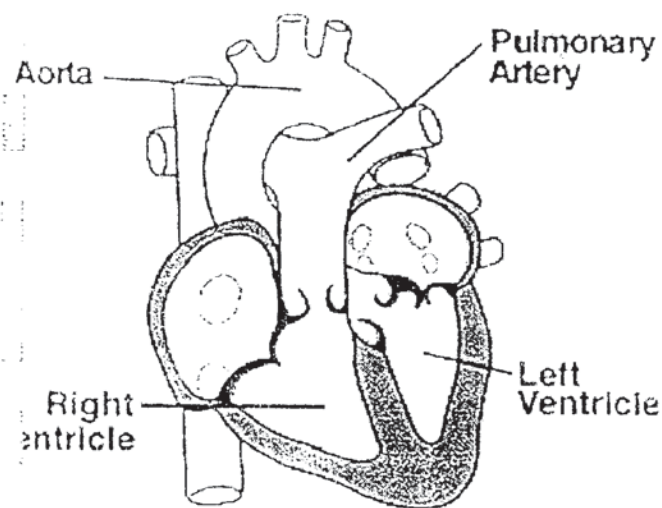
Treatment

1. Protect against infective endocarditis.
2. Propranolol 1mg / Kg / 6hrs $\Rightarrow$ to prevent cyanotic spells.
3. Cyanotic spells.
 - a. Put the patient in squatting position.
 - b. O_2 for correction of anoxia.
 - c. $NaHCO_3$.
 - d. Inderal IV 0.1-0.2 mg / kg $\Rightarrow$ relax the infandibular spasm.
 - e. Morphine (0.2 mg/kg) $\Rightarrow$ in resistant cases.
4. Iron therapy.
5. Surgical:
 - a. Palliative $\Rightarrow$ pulmonary systemic anastomosis e.g. Blalock-Taussing operation between Lt pulmonary & Lt subclavian artery.
 - b. Brock operation = infandibular resection.
 - c. Correction through open heart surgery.



Transposition of Great Arteries

- In this condition the aorta arises from the Rt ventricle & the pulmonary artery from the Lt ventricle. So, non oxygenated blood enters the systemic circulation.
- Survival depends on the mixing between systemic & pulmonary circulations commonly via patent foramen ovale or ASD & PDA.
- In early infancy, the patient's condition may deteriorate when the DA closes.
- C/P: The baby is healthy at birth but becomes persistently cyanosed within the 1st day of birth. Later signs of P++ develop, and if neglected HF will occur.
- X-ray: Egg on side appearance of cardiac shadow.



Rheumatic Fever

Etiology

- It is an auto-immune disease related to throat infection by streptococcus hemolyticus through one of the following mechanisms:
 1. Fixation of streptococcal toxins into tissue proteins rendering them antigenic, and stimulate antibody formation against them.
 2. Antibodies formed against streptococcal antigen are immunologically identical to antigenicity of the heart.

Predisposing Factors

1. Age: 5-15 years (rare below 3 years or above 25 years).
2. Sex: equal (Chorea common in females)
3. Familial tendency.
4. Season: cold months.
5. Over crowding & bad hygienic conditions.
6. Recurrent streptococcal infection.

Clinical Picture

Modified Jonne's criteria

A. Major	B. Minor
1. Arthritis 2. Carditis. 3. Chorea. 4. Erythema marginatum 5. Subcutaneous nodule	1. Fever 2. History of rheumatic fever or rheumatic heart disease. 3. Arthralgia 4. +ve acute phase reactants 5. Prolonged P-R interval

C. Evidence of streptococcal infection

1. Recent scarlet fever
2. +ve throat cultures
3. ↑ ASOT & other streptococcal antibodies

Rheumatic fever can be diagnosed if there are

- Or:
- ** 2 major + evidence of streptococcal infection.
 - ** 1 major + 2 minor + evidence of streptococcal infection

N.B :

- 1) If arthritis is present ⇒ arthralgia is not a minor.
- 2) If carditis is present ⇒ prolonged P-R interval is not a minor.
- 3) Rheumatic chorea may not be accompanied by other manifestations or evidence of streptococcal infection !

1. Carditis:

A. Pericarditis "Dry"	B. Myocarditis	C. Endocarditis
1. Stitching pain 2. Pericardial rub	1. Tachycardia out of fever 2. Gallop rhythm 3. Muffled heart sounds. 4. Dilatation of the ring ⇒ incompetent valves 5. HF in severe cases. 6. <u>ECG</u> : P-R interval 7. <u>CXR</u> : dilated heart	1. Edema of the mitral valve ⇒ MS ⇒ transient mid-diastolic murmur <u>Carey comb's</u> murmur. 2. Destruction & deformity ⇒ MI ± AI 3. On previous Rh heart ⇒ change of character of previous murmur or appearance of new murmur

2. Arthritis:

- Usually large joints e.g. knees, ankle hip, shoulder, elbow or wrist.
- Involved joints become ⇒ red, hot, swollen, tender + loss of function.
- Fleeting arthritis.
- Leaving no residual damage or deformity
- Responds rapidly to salicylates

3. Chorea:

Due to involvement of basal ganglia "Caudate nucleus"

- Common in females around age of puberty.
- It may present alone without other major or minor manifestations.
- Character: Involuntary, semi-purposeful, sudden jerky movements of all limbs, face & tongue.
- Increased by emotions & excitement & disappear during sleep.
- Hypotonia & hyporeflexia are usually associated.
- Emotional instability is usually present.
- Course: self limited or prolonged

4. Subcutaneous nodules:

- Painless, freely mobile under the skin.
- Site ⇒ most commonly over the extensor surfaces & bony prominence as elbows, knees, chin of tibia & mastoid process.

5. Erythema marginatum

- Rings of erythema, with clear center & irregular border.
- Site ⇒ on the trunk.
- They are not painful, not itchy & not scaly.
- They extend to coalesce together with central fading of erythema.

Investigations:1. Acute phase reactants.

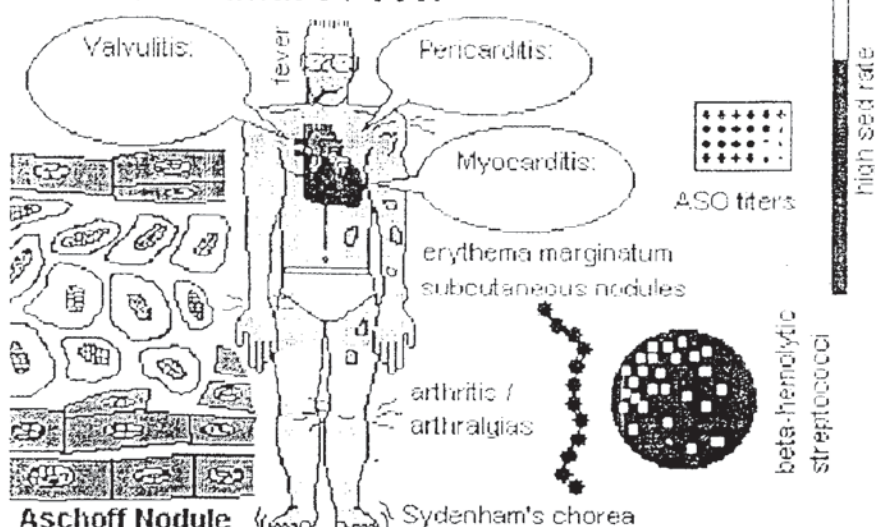
- Leucocytosis.
- ↑↑ ESR
- C-Reactive protein +ve.

2. ECG ⇒ prolonged P-R interval & tachycardia.3. Evidence of previous streptococcal infection

- ↑↑ ASOT > 250 Todd's unit.
- ↑↑ Other streptococcal antibodies.

4. X-ray chest & heart. ⇒ Cardiomegaly.5. Throat culture ⇒ group A, beta hemolytic streptococci may still be present.6. Echo-cardiography: ⇒ Evidence of pancarditis & valvular affection.

Acute Rheumatic Fever



Treatment

A. Prophylaxis

a. Prevention of 1st attack:

1. Proper hygiene to prevent streptococcal infections. This includes good housing, avoiding over crowding, good nutrition, & avoid contact with infected children.
2. Early detection & proper TTT of streptococcal throat infections.
 - The course of TTT should be at least 10 days, using procaine penicillin or erythromycin.
 - A single IM injection of long acting penicillin is advised by some authors.

b. Prevention of 2nd attack of Rh. fever:

Prophylaxis against streptococcal infections for.

- At least 5 years after the last attack.
- Up to 25 years if there's cardiac lesion.
- Some authors recommend continuation for Life.

The drugs used are:

- Long acting penicillin 1.2 million units / 2 weeks.
- Oral penicillin V (Ospen) $\Rightarrow$ 250.000 IU once or twice / day
- Erythromycin 250 mg twice/ day.
- Sulfadiazine 0.5-1 gm once / day.

c. Prevention of infective endocarditis:

1. Procedures which predispose to bacteremia. e.g. tooth extraction, tonsillectomy, catheterization $\Rightarrow$ should be done under an umbrella of antibiotics in all patients with history of rheumatic or congenital heart diseases. $\Rightarrow$ Crystalline penicillin 250.000 IU + procaine penicillin 600.000 IU by IMI one hour before operation. $\Rightarrow$ Then $\Rightarrow$ penicillin V 250.000 — 500.000 IU / 8hrs for 2 days oral.

Recently

- Oral amoxicillin 50 mg/kg 1hr before the procedure & 25 mg/kg 6hrs after the initial dose.
- If there's penicillin allergy $\Rightarrow$ Erythromycin 20 mg/kg 2 hrs before the procedure & 10mg / kg 6hrs after..

Infective Endocarditis

Infection of endocardium may be due to bacteria, rickettsiae or fungus.

Classification

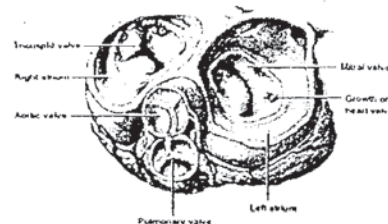
A. Sub-acute form "SBE"

- Caused by low virulent organism.
- Affects diseased heart.

B. Acute form "ABE"

- Caused by highly virulent organism.
- Affects normal & diseased heart.

Infective endocarditis is an infection of the heart chambers or valves



Etiology

There is combination of 2 factors:

Bacteremia	Underlying cardiac lesion
The causative organism 1. Streptococcal viridians "50%" 2. Streptococcal fecalis 3. Staphylococcus aureus $\Rightarrow$ may affect normal heart. 4. G-ve bacteria common in neonates & IV drug abusers. The most common is H-influenza. The Root of infection 1. Dental extraction 2. GIT & urinary procedure. 3. Cardiac surgery.	Congenital: $\Rightarrow$ VSD, PDA & coarctation of the aorta Rare $\Rightarrow$ ASD why? Rheumatic $\Rightarrow$ MI, AS & AI. Rare $\Rightarrow$ MS $\Rightarrow$ why? Prosthetic valves

Fungal endocarditis:

It is due to Candida albicans, aspergillus species etc.

Population affected are:

- Post cardiac surgery.
- Narcotics.
- Immune-compromised patients.
- Neonates with prolonged use of IV catheters.

Pathogenesis

2 factors are needed for the formation of vegetations.

High pressure source	Narrow orifice
So, it is more common in Lt sided heart lesion & rare in: • Heart failure. • MS • ASD	So It is more common in small than big VSD

Clinical Picture

Triad

- A. Embolic manifestations.
- B. Toxemic manifestations.
- C. Underlying cardiac lesion.

A. Toxemic Manifestations

- **Fever** $\Rightarrow$ continuous or intermittent fever of long duration

It may be high grade but the most common low grade fever.

Pediatrics

17

cardiology

- Anorexia, general weakness & loss of weight
- Marked pallor & toxic facies.
- Eyes:

- Roth spots.
- Subconjunctival hge.

- Hands

- Pale clubbing
- Splinter hge in the nail beds
- Osler's nodules: Small, tender, intra-cutaneous nodules in pulps of the fingers, opposite the heads of metacarpal bones
- Jane way nodules ⇒ small painless, blue on the palms & soles.



These lesions represent vasculitis produced by circulating antigen antibody complexes.

- Spleen

Slightly enlarged, soft & tender

B. Underlying cardiac lesion

- Change in the character of the already present murmur
- Development of new murmur.
- Rupture cusps or chorda tendinae ⇒ loud musical murmur "Seagull murmur".
- Endocarditis may precipitates HF

C. Embolic manifestations

The vegetations are easily detached ⇒ septic or aseptic emboli which may lead to:

1. Infarction: if end artery is affected.
2. Ischemia: if non end artery is affected.
3. Mycotic aneurysm due to low grade infected emboli.
4. Renal affection:
 - Flea bitten kidney ⇒ Microscopic hematuria
 - Acute glomerulonephritis ⇒ RBCs cast
 - Infarction ⇒ profuse hematuria.

Complications

1. Embolization.
2. Renal affection ⇒ renal failure.
3. HF due to extensive endocarditis.

Investigations

1. Blood culture & Sensitivity.

3 samples for aerobic, anaerobic bacteria & fungi.

2. CBC: Leukocytosis & Anemia.

3. ESR

4. Urine analysis: Hematuria.

5. Echo-cardiography: To see the vegetations.

Treatment

A. Prevention ⇒ see rheumatic fever.

B. Curative

Antibiotic TTT for at least 4-6 weeks according to culture & sensitivity

- a. It must be bactericidal
- b. Big doses are needed by IVI.

- A combination of penicillin G 200,000 IU / kg / day IV & gentamycin 2-4 mg / kg / day IV.
- If the organism is resistant to penicillin give nafcillin 200 mg / kg / day IV or Vancomycin 40 mg / kg day IV or 3rd generation cephalosporin's.

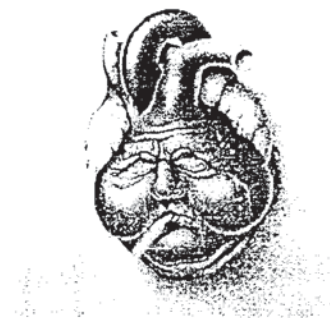
Heart Failure

Definition

- Failure of the heart to supply the tissues with their needs of blood & oxygen.

Etiology

- HF occurs as a result of
 - Pressure overload
 - Volume over load
 - Myocardial disease.



1. Congenital heart diseases

- Large left to right shunt : VSD, ASD & PDA.
- Right & left side obstructive lesions: PS, AS & coarctation of the aorta.
- Congenital valve defect: congenital MI.
- "N.B." It is very rare in F4.

2. Acquired valvular lesions: usually 2ry to rheumatic endocarditis e.g. MS, MI AS, AI.

3. Carditis

- Rheumatic ⇒ most common after 5Y.
- Viral myocarditis ⇒ Coxsackie B virus "commonest"
- Toxic myocarditis ⇒ Pneumonia, Septicemia, Diphtheria & Typhoid.
- Infective endocarditis.

4. Arrhythmias: either tachyarrhythmia (e.g. supraventricular tachycardia & atrial fibrillation) or bradyarrhythmia (e.g. complete heart block).

5. High cardiac output ⇒ severe anemia, thyrotoxicosis, A-V fistula.

6. Cardiomyopathy & endocardial fibroelastosis.

7. Hypertension & pulmonary embolism.

8. Corpulmonale as in cases of cystic fibrosis & bronchopulmonary dysplasia.

9. Fluid overload particularly in the newborn.

Clinical Picture

Depends on the severity of failure.

In infants:

Symptoms:

- Tachypnea & feeding difficulty.
- Poor weight gain.
- Excessive perspiration.
- Irritability & weak cry.

Signs:

- Signs of respiratory distress.
- Tender hepatomegaly.
- Generalized edema more in the eye lids.
- Heart: tachycardia, gallop rhythm + original cardiac lesion.

In children:

1. Low C/O symptoms & signs.

- Easy fatigability.
- Lack of concentration.
- Syncopal attacks.

- Oliguria.
- Intermittent claudication.
- Rapid weak pulse.
- Pale cold extremities.

2. Congestive lung symptoms & signs (in LVF only).

- Cough & expectorations.
- Dyspnea, orthopnea & paroxysmal nocturnal dyspnea.
- Hemoptysis.
- Repeated chest infections.
- O/E: Basal consonating crepitation on the basal part of the lung,

3. Manifestations of systemic venous congestion (in RVF).

- Dyspepsia & vomiting.
- Pain in the right hypochondria.
- Edema in both lower limbs.
- O/E:
 - a. Congested pulsating neck veins.
 - b. Enlarged tender liver.
 - c. Pitting edema in both LL.
 - d. Generalized anasarca in severe cases.

4. Gallop rhythm & findings of the original lesion on auscultation.

Investigations

For diagnosis of underlying cardiac lesion & assessment of cardiac functions.

1. CXR.

- Cardiomegaly.
- ↑↑ Pulmonary vascularity in shunts.
- Pulmonary edema in severe cases: fluffy pulmonary markings of venous congestion & acute pulmonary edema.

2. ECG: helps in diagnosis of specific chamber enlargement.

3. Echocardiography: helps in assessment of myocardial function & diagnosis of underlying lesion.

4. Arterial blood gases.

5. Electrolytes especially Na & K.

Treatment

I. General:

- a. Complete rest in bed: in semi-sitting position.
- b. Salt free diet.
- c. O₂ inhalation.
- d. Treatment of underlying-etiology.

II. Diuretics:

- *Frusemide (Lasix)*: 1-2 mg/kg dose IV or 1-4 mg / kg / day oral. + K syrup. (mechanism of action: loop diuretics ⇒ ↓ volume overload ⇒ ↓ work of the heart, ↓ edema & congestion.)
- *Spironolactone (Aldactone)*: 2-3 mg / kg / day oral. (K-sparing).
- *Chlorthiazide*: 20-40 mg / kg / day.
- Mechanism of action: ↓↓↓ volume over-load → ↓↓↓ work of the heart.

IV. Digitalis: see t t t of rheumatic fever.

Mechanism of action:

- +ve inotropic.
- Slow AV conduction.

V. Vasodilators:

- Na nitroprusside: 0.5-8ug/kg/min IVD in ICU. (↓↓ pre & after load).
- Captopril: 0.5-6 mg / kg / day oral (ACE inhibitor → ↓↓ aldosterone → ↓↓↓ after-load).
- Hydralazine: 0.5 mg / kg IV or oral 0.5-0.75 mg / Kg / D. (↓↓↓ after-load).

VI. Cardiac stimulants:

- Isoproterenol: 0.01-0.05 ug /kg / min IVD in ICU only. (β adrenergic effect & improve myocardial contractility & ↓ after-load).
- Dopamine: 2-20 ug / kg / min IVD in ICU only (as isoproterenol + renal vasodilator).
- Dobutamine: 2-20 ug / kg / min IVD in ICU only.

Mechanism of action: β adrenergic effect → ↑↑↑ myocardial contractility.

VII. Treatment of the underlying cause.

Primary cardiomyopathy

It is a heart muscle disease in the absence of CHD, hypertension, acquired valve lesions, abnormal coronaries, infection or other systemic disease.

Types

1. Hypertrophic cardiomyopathy (AD).

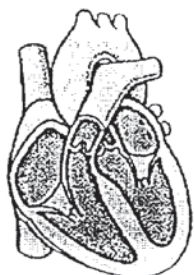
- There is left ventricular hypertrophy associated with hypertrophy of the IVS → obstruction of outflow of LV → dyspnea, PND, chest pain, syncope, palpitations & sudden death.
- TTT: β-blockers & Ca channel blockers.

2. Dilated cardiomyopathy (commonest) (multifactorial? viral).

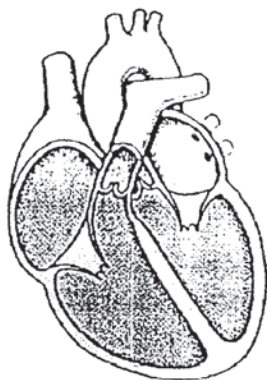
- There is poor contracting myocardium with low COP & CHF.
- TTT: as HF.

3. Restrictive cardiomyopathy,

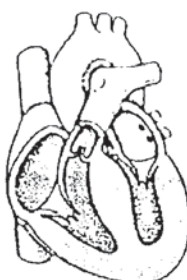
- There is poor ventricular compliance & inadequate filling.
- It has poor prognosis.



Normal



Dilated
Cardiomyopathy



Hypertrophic
Cardiomyopathy



Restrictive
Cardiomyopathy

Secondary Cardiomyopathy

I. Heredo-familial:

1. Duchene myopathy.
2. Becker's myopathy.
3. Friedreich's ataxia.

II. Infections:

1. Virus: Cocksackie's A & B, adenovirus.
2. Rickettsiae.
3. Bacteria: diphtheria, TB & typhoid.
4. Parasitic: Toxoplasmosis.
5. Fungi.

III. Metabolic, nutritional & Endocrinal:

1. Beriberi.
2. KWO.
3. MPS.
4. Hypo & hyperthyroidism.
5. Infant of diabetic mother.

IV. Connective tissue, granulomatous & infiltrative:

1. SLE.
2. JRA.
3. Rheumatic fever.
4. Sarcoidosis.
5. Leukemia.

V. Drugs & toxins:

1. Adriamycin.
2. Hemosiderosis.
3. Irradiation.

VI. Coronary artery diseases:

1. Congenital.
2. Kawasaki.

VII. Others:

1. Anemia.
2. Sickle cell anemia.

		VSD	F4	ASD
Symptoms		1- Asymptomatic 2- Congestive lung symptoms 3- Palpation 4- Low CO symptoms 5- Cyanosis on crying (+/-)	1- Cyanosis: starts shortly after birth 2- Clubbing 3- Squatting position 4- Cyanotic spells	1- Symptomatic 2- Congestive lung symptoms 3- Palpitation 4- Cyanosis after reversal of shunt
Signs	Inspection and palpation	1. Pericardial bulge. 2. Apex: - Site: shifted down and outward - Size: diffuse - Character: hyper dynamic - Thrill: systolic 3. Lt. para-sternal pulsations. 4. Epigastric pulsations. 5. Diastolic shock over the pulmonary area in case complicated by P++	1. Pericardial bulge. 2. Apex: - Site: may be shifted outwards. - Size: may be diffuse. - Character: normal 3. Lt. parasternal pulsations (±) 4. Epigastric pulsations (±) 5. No thrill pulsations over the pulmonary area.	1. Pericardial bulge. 2. Apex: - Site: shifted outwards. - Size: diffuse. - Character: hyper dynamic. 3. Lt. and Rt. Parasternal pulsations. 4. Epigastric pulsations. 5. Diastolic shock: over the pulmonary area in cases complicated by P++.
	Percussion	Dullness over the pulmonary area in cases complicated by P++	The pulmonary area is resonant	Dullness over the pulmonary area in cases complicated by P++
	Auscultation	1- S1: normal 2- S2: accentuated in cases complicated by P++ 3- Harsh, pan-systolic murmur maximum over the Lt. 3rd & 4th para-sternal area propagated all over the pericardium.	1. S1: normal 2. S2: single and accentuated. 3. Harsh, ejection systolic murmur, maximum over the pulmonary area, propagated to the Lt. parasternal area.	1. S1: normal. 2. S2: wide, fixed splitting. 3. Soft, ejection systolic murmur, maximum over the pulmonary area, may be propagated to the Lt. Parasternal area (functional PS)

Complications	1. Repeated chest infections 2. Congestive heart failure. 3. Infective endocarditis 4. Isenminger syndrome 5. Stunted growth	1. Cyanotic spells. 2. Pulmonary TB. 3. Polycythemia → thrombosis 4. Cerebral thrombosis 5. Brain abscess 6. Infective endocarditis & HF. 7. Stunted growth	1. Repeated chest infections. 2. Congestive HF. 3. Infective endocarditis 4. Isenminger syndrome 5. Stunted growth.
Investigations	1. CXR. 2. ECG. 3. Echocardiography. 4. Cardiac catheterization.		
Treatment	Medical	Prophylaxis against SBE.	1. Prophylaxis against SBE. 2. Propranolol: 1 mg/kg as prophylaxis against cyanotic spells. 3. Cyanotic spells: - a- Put the patient in squatting position. - b- O2 therapy. - c- NaHCO₃ - d- Propranolol IVI - e- Morphine in resistant cases.
	Surgical	1- Membranous regardless the size. 2- Large muscular. 3- Increasing pulmonary artery pressure. 4- After the age of 5 years.	- A- Palliative: 1- Blalock-Taussing. 2- Brock - B- Total correction . Surgical closure of large defect

		PDA	MS	MI
Symptoms		1. Asymptomatic 2. Low CO symptoms (in LL) 3. Congestive lung symptoms 4. Palpitation. 5. Differential cyanosis (in LL) on reversal of shunt.	1. Asymptomatic in mild cases. 2. Congestive lung symptoms. 3. Low CO symptoms (hypertensive type) 4. Symptoms of systemic venous congestion in cases complicated by RVF.	1- Asymptomatic 2- Palpitation 3- Low CO symptoms 4- Congestive lung symptoms.
Signs	Inspection and palpation	1- Apex: - Site: shifted downwards and outwards. - Size: localized. - Character: hyper dynamic 2- Diastolic shock over pulmonary area in cases complicated by P++ 3- Continuous thrill over the Lt. infra-clavicular area.	A- General: 1. Absent in mild cases. 2. Fine basal crepitations in congestive MS. 3. Malar flush in hypertensive MS. 4. Congested neck veins, enlarged tender liver in stage IV. B- Local: 1- Apex: - Site: may be shifted outwards. - Size: diffuse. - Character: slapping. - Diastolic thrill 2- Parasternal pulsations 3- Epigastric pulsations 4- Diastolic shock over the pulmonary area in cases complicated by P++.	A- General: As in MS except malar flush. B- Local: 1- Apex: - Site: shifted downward and outward - Size: localized. - Character: hyper dynamic. - Systolic thrill: 2- Diastolic shock over the pulmonary area in cases complicated by P++.
	Percussion	Dullness over the pulmonary area in cases complicated by P++	Dullness over the pulmonary area in cases complicated by P++	Dullness over the pulmonary area in cases complicated by P++

	Auscultation	1- S1: normal 2- S2: accentuated in case complicated by P++. 3- Continuous machinery murmur, maximum over the Lt. infra-clavicular area, propagated to the pulmonary area.	1- S1: accentuated. 2- S2: accentuated in cases complicated by P++. 3- Mid-diastolic rumbling murmur, maximum over the apex and may be propagated to the inner side of the apex.	1- S1: muffled. 2- S2: accentuated in cases complicated by P++ 3- Soft, pan-systolic murmur, maximum over the apex, propagated to the axilla.
	Complications	1. Repeated chest infections 2. Congestive heart failure. 3. Infective endocarditis 4. Isenminger syndrome 5. Stunted growth	A- Valve: 1- RH-activity. 2- SBE. 3- Calcifications B- Lt. atrium: 1- AF. 2- Pressure manifestations. 3- Thrombo-embolism. C- Lung: 1- Repeated chest infection. 2- Hemoptysis. 3- Pulmonary infarction. D- RVF. 1. CXR. 2. ECG. 3. Echocardiography.	As MS
Investigations		1. CXR. 2. ECG. 3. Echocardiography. 4. Cardiac catheterization	1. CXR. 2. ECG. 3. Echocardiography.	As MS
Treatment	Medical	1- Prophylaxis against SBE. 2- Endomethacin early in the neonatal period.	1- Prophylaxis against SBE. 2- Prophylaxis against rheumatic fever.	As MS
	Surgical	Surgical closure even if small	1- Dilatation in pure non-calcified MS. 2- Valve replacement if there is calcifications or MI.	Valve replacement

		AS	AI
Symptoms		1- Asymptomatic in mild cases. 2- Low CO symptoms. 3- Anginal pain. 4- Congestive lung symptoms if complicated by LVE.	As AS + palpitation
Signs	General	1- Plateau pulse. 2- Systolic thrill over the carotid arteries.	1- Water hammer pulse. 2- De-Musse sign. 3- Corrigan's signs. 4- Prominent capillary pulsations. 5- Pistol shot.
	Inspection and palpation	1. Apex: - Site: shifted downward and outward. - Size: localized. - Character: heavy sustained. 2. Systolic thrill over the 1 st aortic area.	<u>Apex:</u> - Site: shifted downward and outward. - Size: localized. - Character: hyper dynamic. - Diastolic thrill.
	Percussion	Dullness on the 1 st aortic area due to post-stenotic dilatation.	Non-specific
	Auscultation	1. S1: normal 2. S2: muffled. 3. Harsh ejection systolic murmur, maximum over the 1 st aortic area, propagated to the apex and neck.	1. S1: normal. 2. S2: muffled. 3. Soft, early diastolic murmur, maximum over the 2 nd aortic while the patient is leaning forward.
Complications		As valve complications of MS + myocardial infarction	As valve complications of MS + LVE
Investigations		As MS	As MS
Treatment	Medical	As MS + propranolol for IHSS	As MS + TTT of syphilitic AI
	Surgical	1- Dilatation in pure non-calcified AS. 2- Valve replacement if there is calcifications or AI. 3- Resection for IHSS.	Valve replacement

Chest

CROUP = stridor

Definition

- It is a group of ^{clinical} acute conditions characterized by **croupy cough** which may or may not be associated with:

- 1- Inspiratory stridor.
- 2- Hoarseness of voice.
- 3- Signs of respiratory distress. (±) 2 or 3.

Etiology

1- Laryngeal obstruction

- 1- Mechanical
- Congenital web.
 - Laryngeal or tracheomalacia.
 - FB. (اشهر واحة)
 - Laryngeal stenosis.

2- Inflammatory

- viral Para-influenza, RSV, Measles and adenovirus →
- Acute laryngotracheo-bronchitis
 - Acute spasmodic croup.
 - H. influenza → acute epiglottitis.
 - Diphtheria.

3- Laryngismus stridulus → due to hypocalcaemia. urticary → affection of abductors of vocal cord

4- Angio-neurotic edema.

5- Laryngeal papilloma.

6- Others:

- Goiter and retropharyngeal abscess.

Clinical Picture

- 1- Croupy cough → characteristic.
- 2- Inspiratory stridor.
- 3- Hoarseness of voice.
- 4- Marked respiratory distress "Inspiratory": → due to laryngeal obstruction.
- 5- Cyanosis may occur.
- 6- Constitutional manifestations e.g. high fever and toxemia and drooling of saliva especially in epiglottitis.

Radiological Findings

1- lateral neck film:

Show subglottic narrowing and normal epiglottis in acute laryngotracheo-bronchitis.

2- PA view:

Shows classic narrow trachea (Wine bottle sign) in acute laryngo-tracheo-bronchitis.

- 3- In acute epiglottitis, edematous epiglottis can be seen in lateral view neck.

4 * Radiopaque F.B.



Treatment

Emergency

"Never endotracheal tube"

1- Treatment of the cause

- Epiglottitis → 3rd generation cephalosporin.
- Diphtheria → penicillin, antitoxins.
- Hypocalcaemia → IV infusion of Ca-gluconate
- FB → bronchoscopic removal.

2- Cold humidified O2 inhalation

3- **Racemic epinephrine** (2.5% solution) delivered by nebulizer, helps to improve air exchange.

4- Steroids

- Dexamethasone 0.5 mg/kg for 1-3 doses in severe cases. • No max. dose in Croup.

5- Endo-tracheal intubations or tracheostomy:

- In severe cases may be needed.

- Acute spasmodic laryngitis (spasmodic cough)

It is brief repeated attacks of croup but less severe, mostly in children 1-3 years old. Probably it is allergic in nature, TTT is at home with humidified air. • like Asthma.

humified O2 inhalation

Bronchiolitis

- It is common disease of infants affecting terminal bronchioles.
- **Age:** during 1st 2 years of life with peak incidence in the 1st 6 months of age.
- **Season:** winter and early spring.

Etiology

- 1- RSV → the commonest (50%)
- 2- Para-influenza virus.
- 3- Mycoplasma.
- 4- Adenovirus.
- 5- Herpes & rhinovirus.

Clinical Picture

- 1- URT catarrhal symptoms and fever → it usually starts with mild to moderate fever (38-39) with nasal discharge and sneezing.
- 2- Then gradual development of:
 - Paroxysms of cough. may productive
 - Dyspnea.
 - Wheeze.
 - Cyanosis.

Examination

1- inspection:

- Tachypnea and working ala nasi.
- Intercostals and subcostal retraction.
- Cyanosis → in severe cases.
- Limitation of movement of the chest bilateral.
- **Barrel-shape chest.** • Bilat. pulse ...

2- Palpation:

- Central trachea.
- **Palpable wheeze.**



humified O2 inhalation



Catarrhal oedema
↓
Narrowing of Bronchioles

بيل 500 يدقل هوا 300 يس

الدنيا يضيق أكثر في الـ Exp.
← ينزح 200 يس

hyperinflation

• Bilat. → as dis is system

• Barrel shape chest

• hyperresonance

Complications

• Resp. P.

• P. P.

• post viral autoimmune.

3- **Percussion:**

- Bilateral **hyper resonant** chest.

4- **Auscultation:**

- Bilateral **diminished** air entry.
- **Harsh vesicular** breathing.
- Bilateral **sibilant ronchi** and **fine or medium-sized consonating crepitations** all over the chest.

→ to differentiate from viral pneumonia

لواء الحاله انثرت

Investigations

- 1- **CXR:** hyper-inflated chest.
- 2- **CBC:** leucocytosis "**lymphocytosis**".
- 3- **Sputum C & S:** if 2ry infection is suspected.
- 4- **Blood gases:** to exclude **Respiratory failure**.
- 5- **Viral markers** and viral isolation.



Treatment

- 1- **Hospitalization**
- 2- **Cold humidified O2.**
- 3- **IV fluids** 2/3rd maintenance.
- 4- **Relavir** as antiviral drug especially against influenza virus.
- 5- **Antibiotics:** have no role except if there is **2ry bacterial infection**.
- 6- **In severe cases:**

- Corticosteroid: e.g. hydrocortisone 10 mg/dose/6hours IV (some authors refuse cortisone).
- $\beta 2$ agonist inhaler "nebulizer" *sympathomimetic*
- Correction of acidosis $\rightarrow$ NaHCO_3 .
- TTT of heart failure $\rightarrow$ digitalis.
- Mechanical ventilation may be needed.

النبي ليد
سه الا قواس

Pneumonia

Definition

- Infection of the **lung parenchyma**

Classification

A. Anatomical

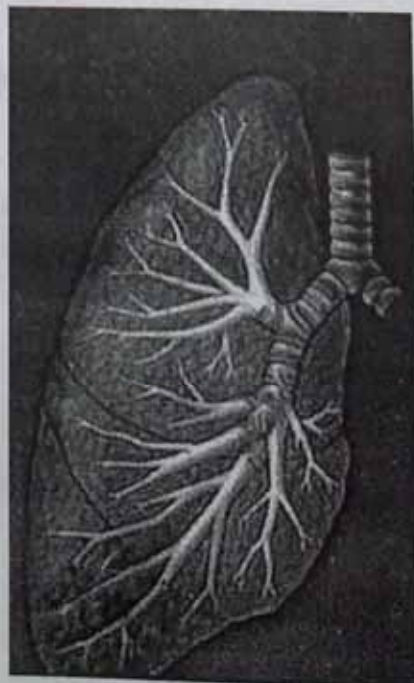
- Bacterial* a- Lobar pneumonia
- b- Bronchopneumonia *pneumonic patches around bronchi*
- Viral* c- Interstitial pneumonia. *→ Hilum*

B. Etiological:

1- **bacterial:**

- **Gm +ve**
 - Pneumococci.
 - Streptococci.
 - Staphylococci.
- **Gm -ve**
 - H. influenza.
 - Klebsiella.
 - Pseudomonas aerogenosa.
- **Acid-fast** $\rightarrow$ TB
- Others chlamydia pneumonia

2- **Viral:** RSV – adovirus- Influenza virus



- 3- **Parasitic infestation:** pneumocystic carinii.
- 4- **Chemical:** due to hydrocarbon inhalation → CT 2. ④ → aspiration during surgery
- 5- **Physical** → sudden change in Body Temp. → الحمى والبرودة
- 6- **Hypostatic pneumonia**
- 7- **Aspiration**
 - Amniotic fluid.
 - Food.
 - FB.
 - Lipoid substance.
- 8- **Radiation pneumonia** → Radiation affects lung parenchyma
- 9- **Hypersensitivity** to hay and dust of air conditioning.
- 10- **Mycoplasma pneumoniae.**

Clinical Picture of Pneumonia in general

❖ Symptoms

- 1- Fever: high grade fever in bacterial infection and low grade in others.
- 2- Cough.
- 3- Expectoration.
- 4- Dyspnea. → صعوبة التنفس
- 5- grunting.
- 6- Chest pain → if there is overlying pleurisy. "stitching pain".
- 7- Cyanosis. "Respiratory".

❖ Signs

The general clinical signs of pneumonia

1- **Inspection**

- Tachypnea and working ala nasi.
- Intercostals and subcostal retraction.
- Expiratory grunting.
- Cyanosis in severe cases.
- Limitation of chest movement according to the site of the lesion.

2- **Palpation**

- Central trachea.
- ↑↑↑ TVF. on affected parts.
- Palpable pleural rub if there is overlying pleurisy.

3- **percussion**

- Dullness over the affected lobe in lobar and bilateral, patchy in bronchopneumonia and interstitial pneumonia. "Pleurisy → Tender Perc"
- Percussion is tender if there is overlying pleurisy.

4- **Auscultation:**

- 1 - Diminished air entry.
- 2 - Bronchial breathing. , Bronchophony → جرس
- 3 - Fine & medium sized consonating crepitations. خفيف
- 4 - Pleural rub if there is overlying pleurisy.

All these findings are bilateral in bronchopneumonia and over the affected lobe in lobar pneumonia.

Complications:

4 complications should be excluded in every case:

1- **Pleural effusion:**

- Mostly seen in infants & young children with severe bacterial pneumonia

2- Respiratory failure:

- It is mainly seen in infants with severe pneumonia
 - $PO_2 < 50$ mmHg.
 - $PCO_2 > 60$ mmHg.
 - $PH < 7.2$.

3-HF:

- Common with severe bacterial pneumonia, mostly due to
 - Toxic myocarditis in bacterial pneumonia:
 - Viral myocarditis in viral pneumonia

5- Paralytic or toxic ileus:

→ القولنج السام ← organism
Toxin

Investigations**1- CBC**

- $\uparrow\uparrow\uparrow$ WBCs mostly neutrophilia in bacterial infection or lymphocytosis in viral infection & TB. + polycythemia.

2- CXR → It is important:

- To identify the pathological type

- Lobar.
- Bronchopneumonia.
- Interstitial.

- To detect complications as:

- Cardiomegaly
- Pleural effusion
- Pyopneumothorax.

3- Blood gases to evaluate the respiratory function.**4- Others** → to identify the causative agent e.g.

- Culture from
 - Sputum.
 - Blood.
 - Pleural tap.



pneumonia

Treatment**1- Hospitalization**

- Is needed in cases with marked RD or complications for supportive care
 - O₂ therapy.
 - Fluid intake.
 - Bed rest.

2- Symptomatic ttt

- Fever → Aspirin or paracetamol 15 mg/kg/dose.
- Expectorant & mucolytics.

3- Specific ttt:**a- Pneumococci**

- Penicillin is the drug of choice for 7-10 days in uncomplicated cases.
- In complicated or resistant cases 3rd generations cephalosporin.

b- Staphylococci

- Penicillinase resistant antibiotics are used for 3-4 weeks e.g. Methicillin 200 mg/kg/D IV, Cloxacillin 100mg/kg/D IV.

c- Klebsiella → 3rd generation cephalosporin.**d- Mycoplasma:** Erythromycin, clarithromycin (15 mg / kg / D) & azithromycin are effective drugs.**e- Influenza A:** Ribavirin can be used.

4- ttt of complications:

- Empyema $\Rightarrow$ intercostal tube & drainage under water-seal.
- HF $\Rightarrow$ Diuretics $\pm$ Digitalis 0.01 mg/kg/D.
- Respiratory failure $\Rightarrow$ mechanical ventilator.

Pneumococcal pneumonia

- Most common "90%" more common in winter & early spring.
- Peak age in the 1st 4 years of life.
- * In infants $\Rightarrow$ diffuse bronchopneumonia.
- In childhood $\Rightarrow$ lobar pneumonia.

C/O

- Fever, high grade
- Cough.
- Expectoration.
- Dyspnea.
- Grunting.
- Chest pain $\Rightarrow$ if there is overlying pleurisy.
- Cyanosis.

O/E

❖ Inspection:

- Tachypnea & working alae nasi.
- Intercostal & subcostal retraction.
- Expiratory grunting
- Cyanosis in severe cases.
- Limitation of movement of the chest according to the site of the lesion.

❖ Palpation:

- Central trachea.
- $\uparrow\uparrow\uparrow$ TVF.
- Palpable pleural rub if there is overlying pleurisy.

❖ Percussion:

- Dullness over the affected lobe in lobar & bilateral, patchy in bronchopneumonia
- Percussion is tender if there is overlying pleurisy.

❖ Auscultation

- Diminished air entry.
- Bronchial breathing.
- Fine or medium sized consenting crepitations
- All these findings are patchy all over the chest in bronchopneumonia & over the affected lobe in lobar pneumonia.
- Pleural rub if there is overlying pleurisy.

Complications

1- Pleural effusion:

- Mostly seen in infants & young children with severe pneumonia

2- Respiratory failure: It is mainly seen in infants with severe pneumonia

- $P_{O_2} < 50$ mmHg.
- $P_{CO_2} > 60$ mmHg.
- $PH < 7.2$.

3- **HF:**

- Common with severe pneumonia:
- Mostly due to toxic myocarditis.

4- **Paralytic or toxic ileus:**

- 5- **Meningism:** toxins pass through paravert. plexus of veins.
 - can occur in upper lobar pneumonia $\Rightarrow$ signs of meningeal irritation as neck rigidity. no inf. cells or org. in lumbar puncture - puncture - ven.

6- **Lung abscess.**

Investigations

1- **CBC:**

- $\uparrow\uparrow$ WBCs mostly neutrophilia

2- **CXR** $\rightarrow$ It is important:

- To identify the pathological type

No interstitial

- Lobar.
- Bronchopneumonia.

- To detect complications as

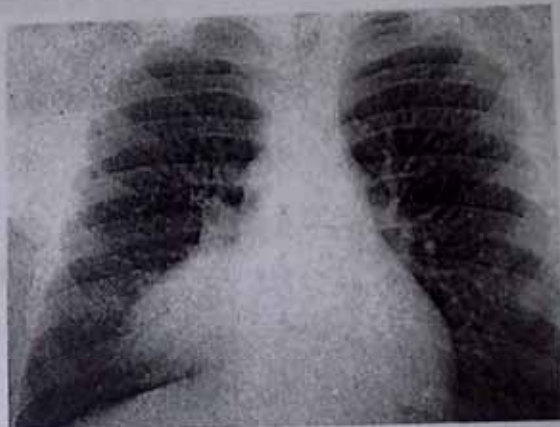
No Pyopneumo

- Cardiomegaly
- pleural effusion.

3- **Blood gases** to evaluate the respiratory function.

4- **Others**

- $\Rightarrow$ to identify the causative agent e.g.
 - Culture from isolation of org....
 - Sputum.
 - Blood.
 - Pleural tap.



Right middle-lobe pneumonia

D.D

1. Other causes of pneumonia.
2. Other causes of respiratory distress.
3. Meningitis.

Treatment

1- **Hospitalization**

- is needed in cases with marked RD or complications for supportive care
 - O₂ therapy.
 - Fluid intake.
 - Bed rest.

2- **Symptomatic ttt**

- Fever $\rightarrow$ Aspirin or paracetamol 15 mg/kg/dose.
- Expectorant & mucolytics.

3- **Specific ttt:**

- Penicillin is the drug of choice for 7-10 days in uncomplicated cases.
Penicillin G 50-100,000 U/kg / D divided every 4-6hrs IV.
- In resistant cases 3rd generation Cephalosporin as Cephtriaxone 150 mg / Kg / day or Cephtriaxone 50-75 mg / Kg / day.
- Polyvalent pneumococcal vaccine $\Rightarrow$ For prevention in susceptible children.

4- **ttt of complications:**

- Empyema $\Rightarrow$ intercostal tube & drainage under water-seal.
- HF $\Rightarrow$ Diuretics $\pm$ Digitalis 0.01 mg/kg/D.
- Respiratory failure $\Rightarrow$ mechanical ventilator.

Staphylococcal pneumonia

- The most serious & most fulminated type.
- Predisposed by staph skin infection & nasal carriers.
- Age $\Rightarrow$ 1 year in 70% of cases.
- Mostly $\Rightarrow$ Unilateral bronchopneumonia, mostly RT.
- Emphysema & pyopneumothorax are very common in CXR.

Purulence in parent skin
" Breast or nose

C/O

- Fever: high grade & toxemia.
- Cough.
- Expectoration.
- Dyspnea.
- Grunting.
- Chest pain $\Rightarrow$ if there is overlying pleurisy.
- Cyanosis.

O/E

- ❖ **Inspection:**
 - Tachypnea & working alae nasi.
 - Intercostal & subcostal retraction.
 - Expiratory grunting.
 - Cyanosis in severe cases.
 - Limitation of movement of the chest (usually unilateral).
- ❖ **Palpation:**
 - Central trachea.
 - $\uparrow\uparrow\uparrow$ TVF.
 - Palpable pleural rub if there is overlying pleurisy.
- ❖ **Percussion:**
 - Dullness, usually unilateral & patchy.
 - Percussion is tender if there is overlying pleurisy.
- ❖ **Auscultation:**
 - Diminished air entry.
 - Bronchial breathing & bronchophony.
 - Fine or medium sized consonating crepitations, unilateral, patchy over the side of chest in bronchopneumonia.
 - Pleural rub if there is overlying pleurisy.

Complications

- 1- **Pleural effusion:**
 - Mostly empyema. *• Pus.*
- 2- **Respiratory failure:**
 - It is mainly seen in infants with severe pneumonia
 - $P_{O_2} < 50$ mmHg.
 - $P_{CO_2} > 60$ mmHg.
 - $pH < 7.2$.
- 3- **HF:**
 - Common with severe pneumonia: mostly due to
 - Toxic myocarditis in bacterial pneumonia.
 - Staph pericarditis.

- 4- Paralytic or toxic ileus
 - ⑤ Multiple lung abscesses
 - if rupture $\Rightarrow$ pyopneumothorax Or erode bronchus $\Rightarrow$ bronchopleural fistula.
 - ⑥ Meningitis.
 - ⑦ Osteomyelitis,
 - ⑧ Metastatic abscesses in soft tissues.
- suppuration every week.
9 + Pneumococci.

Investigations

- 1- CBC
 - $\uparrow\uparrow$ WBCs mostly neutrophilia.
- 2- CXR $\rightarrow$ It is important:
 - To identify the pathological type $\rightarrow$ unilateral Bronchopneumonia.
 - To detect complications as
 - Cardiomegaly, pleural effusion
 - ⑧ Pyopneumothorax.
- 3- Blood gases to evaluate the respiratory function.
- 4- Others
 - to identify the causative agent e.g.
 - Culture from (Sputum, Blood, Pleural tap).

TTT

- 1- Hospitalization
 - is needed in cases with marked RD or complications for supportive care
 - O₂ therapy.
 - Fluid intake.
 - Bed rest.
- 2- Symptomatic ttt
 - Fever $\Rightarrow$ Aspirin or paracetamol 15 mg/kg/dose.
 - Expectorant & mucolytics.
- 3- Specific ttt:
 - Penicillinase resistant antibiotics are used for 3-4 weeks e.g. Methicillin 200 mg/kg/D IV, or Cloxacillin 100 mg/kg/D IV.
 - Cephalosporins as cephazoline: 50mg/Kg/day for 3-4 weeks if there is penicillin allergy.
- 4- ttt of complications:
 - Empyema $\Rightarrow$ intercostal tube & drainage under water-seal.
 - HF $\Rightarrow$ Diuretics $\pm$ Digitalis 0.01 mg/kg/D.
 - Respiratory failure $\Rightarrow$ mechanical ventilator.

*CephaZoline: 3P $\left\{ \begin{array}{l} \text{Parental} \\ \text{Power to penetrate Bone.} \\ \text{Penicillinase Resistant.} \end{array} \right.$

المضاد ليس آمن لمريض في ٣ * (Handwritten note in Arabic)

Group A Streptococcal pneumonia

C/O

- Mostly diffuse bronchopneumonia *may Bilat. , Rarely lobar..*

- Fever: high grade
- Cough.
- Expectoration.
- Dyspnea.
- Grunting.
- Chest pain → if there is overlying pleurisy.
- Cyanosis.

O/E

❖ Inspection:

- Tachypnea & working alae nasi.
- Intercostal & subcostal retraction.
- Expiratory grunting.
- Cyanosis in severe cases.
- Limitation of movement of the chest, according to the site of the lesion.

❖ Palpation:

- Central trachea.
- ↑↑↑TVF.
- Palpable pleural rub if there is overlying pleurisy.

❖ Percussion:

- Dullness over the affected lobe in lobar & bilateral, patchy in bronchopneumonia
- Percussion is tender if there is overlying pleurisy.

❖ Auscultation

- Diminished air entry.
- Bronchial breathing & bronchophony
- Fine or medium sized consonating crepitations patchy all over the chest in bronchopneumonia & over the affected lobe in lobar pneumonia. :
- Pleural rub if there is overlying pleurisy.

Complications

1- Pleural effusion:

- Mostly seen in infants & young children with severe pneumonia

2- Respiratory failure:

- It is mainly seen in infants with severe pneumonia
 - $PO_2 < 50$ mmHg.
 - $PCO_2 > 60$ mmHg.
 - $PH < 7.2$.

3- HF:

- Common with severe pneumonia:
- Mostly due to toxic myocarditis.

4- Paralytic or toxic ileus

5- Post-streptococcal GN or Rheumatic fever

6- Septic foci in bones & joints.

Investigations

- 1- **CBC**: ↑↑↑ WBCs mostly neutrophilia
- 2- **CXR** ⇒ It is important:
 - To identify the pathological type
 - Bronchopneumonia
 - Hilar lymphadenopathy
 - To detect complications as cardiomegaly, pleural effusion.
- 3- **Blood gases** to evaluate the respiratory function.
- 4- **Others** ⇒ to identify the causative agent e.g.
 - Culture from
 - Sputum.
 - Blood.
 - Pleural tap.
- 5- **ASOT**. *Anti streptolysin O Titre.*

D.D

1. Other causes of pneumonia.
2. Other causes of respiratory distress.

TTT

- 1- **Hospitalization**
 - is needed in cases with marked RD or complications for supportive care
 - O₂ therapy.
 - Fluid intake.
 - Bed rest.
- 2- **Symptomatic ttt**
 - Fever ⇒ Aspirin or paracetamol 15 mg/kg/dose.
 - Expectorant & mucolytics.
- 3- **Specific ttt**
 - Penicillin is the drug of choice for 7-10 days in uncomplicated cases.
Penicillin G 50-100,000 U / kg / D divided every 4-6hrs IV.
- 4- **TTT of complications**:
 - Empyema ⇒ intercostal tube & drainage under water-seal.
 - HF ⇒ Diuretics ± Digitalis 0.01 mg/kg/D.
 - Respiratory failure ⇒ mechanical ventilator.

Klebsiella pneumonia

- Caused by Friedlander's bacillus
- Usually occur in debilitating & immunocompromized child. *"School age"*
- Bronchopneumonia or lobar but mostly lobar with cavity formation & bulging fissures.
- It causes Hgic pleural effusion which may be misdiagnosed as malignant disease.

C/O

- Fever.
- Cough.
- Expectoration.
- Dyspnea.
- Grunting.
- Chest pain ⇒ if there is overlying pleurisy.
- Cyanosis.

O/E❖ **Inspection:**

- Tachypnea & working alae nasi.
- Intercostal & subcostal retraction.
- Expiratory grunting.
- Cyanosis in severe cases.
- Limitation of movement of the chest, according to the site of the lesion.

❖ **Palpation:**

- Central trachea.
- ↑↑↑TVF.
- Palpable pleural rub if there is overlying pleurisy.

❖ **Percussion:**

- Dullness over the affected lobe in lobar & bilateral, patchy in bronchopneumonia
- Percussion is tender if there is overlying pleurisy.

❖ **Auscultation**

- Diminished air entry.
- Bronchial breathing & bronchophony
- Fine or medium sized consonating crepitations patchy all over the chest in bronchopneumonia & over the affected lobe in lobar pneumonia.
- Pleural rub if there is overlying pleurisy.

Complications① **Pleural effusion:**

- Mostly Hgic & seen in infants & young children with severe pneumonia

2- **Respiratory failure:**

- It is mainly seen in infants with severe pneumonia
 - $PO_2 < 50 \text{ mmHg}$.
 - $PCO_2 > 60 \text{ mmHg}$.
 - $PH < 7.2$.

3- **HF:**

- Common with severe pneumonia:
- Mostly due to toxic myocarditis.

4- **Paralytic or toxic ileus:****Investigations:**1- **CBC:** ↑↑↑ WBCs mostly neutrophilia.2- **CXR** ⇒ It is important:

- To identify the pathological type
 - Lobar.
 - Bronchopneumonia.
- To detect complications as cardiomegaly, Hgic pleural effusion.

3- **Blood gases** to evaluate the respiratory function.4- **Others** ⇒ to identify the causative agent e.g.

- Culture from
 - Sputum.
 - Blood
 - Pleural tap.

C-X Ray

* Voluminous lobe
w/ inf. oedema.

→ appear as
a mass.

* Puncture: Hgic

eff ⇒ misdiagnosed as a tumor.
"malignancy..."



ITT1- **Hospitalization**

- is needed in cases with marked RD or complications for supportive care
 - O₂ therapy.
 - Fluid intake.
 - Bed rest.

2- **Symptomatic ttt**

- Fever ⇒ Aspirin or paracetamol 15 mg/kg/dose.
- Expectorant & mucolytics.

3- **Specific ttt:**

- 3rd generation cephalosporin e.g. Cefotriaxone or Cefotaxime & *G-ve* Aminoglycosides

4- **ttt of complications:**

- Empyema ⇒ intercostal tube & drainage under water-seal.
- HF ⇒ Diuretics ± Digitalis 0.01 mg/kg/D.
- Respiratory failure ⇒ mechanical ventilator.

H-influenza type B pneumonia

C/O

- Fever
- cough
- Expectoration.
- Dyspnea.
- Grunting.
- Chest pain ⇒ if there is overlying pleurisy.
- Cyanosis.

*mostly lobar
sometimes Broncho.*

*G-ve capsulated
organism*

O/E❖ **Inspection:**

- Tachypnea & working alae nasi.
- Intercostal & subcostal retraction.
- Expiratory grunting.
- Cyanosis in severe cases.
- Limitation of movement of the chest, according to the site of the lesion.

❖ **Palpation:**

- Central trachea.
- ↑↑↑TVF.
- Palpable pleural rub if there is overlying pleurisy.

❖ **Percussion:**

- Dullness over the affected lobe in lobar & bilateral, patchy in bronchopneumonia
- Percussion is tender if there is overlying pleurisy.

❖ **Auscultation**

- Diminished air entry.
- Bronchial breathing & bronchophony
- Fine or medium sized consonating crepitations.
- Pleural rub if there is overlying pleurisy.

Complications

- 1- **Pleural effusion:**
 - Mostly seen in infants & young children with severe pneumonia
- 2- **Respiratory failure:**
 - It is mainly seen in infants with severe pneumonia
 - $PO_2 < 50$ mmHg.
 - $PCO_2 > 60$ mmHg.
 - $PH < 7.2$.
- 3- **HF:**
 - Common with severe pneumonia:
 - Mostly due to toxic myocarditis.
- 4- **Paralytic or toxic ileus:**
- 5- **Meningism or meningitis:**
 - can occur in upper lobar pneumonia $\Rightarrow$ signs of meningeal irritation as neck rigidity.
- 6- **Lung abscess.**

Investigations

- 1- **CBC:** $\uparrow\uparrow\uparrow$ WBCs mostly neutrophilia
- 2- **CXR** $\Rightarrow$ It is important:
 - To identify the pathological type
 - Lobar.
 - Bronchopneumonia.
 - To detect complications as cardiomegaly, pleural effusion.
- 3- **Blood gases** to evaluate the respiratory function.
- 4- **Others** $\Rightarrow$ to identify the causative agent e.g.
 - Culture from
 - Sputum.
 - Blood.
 - Pleural tap.

D.D

1. Other causes of pneumonia.
2. Other causes of respiratory distress.
3. Meningitis.

TTT

- 1- **Hospitalization:**
 - is needed in cases with marked RD or complications for supportive care
 - O_2 therapy.
 - Fluid intake.
 - Bed rest.
- 2- **Symptomatic ttt:**
 - Fever $\Rightarrow$ Aspirin or paracetamol 15 mg/kg/dose.
 - Expectorant & mucolytics.
- 3- **Specific ttt:**
 - 3rd generation cephalosporin e.g. Ceftriaxone or Cefotaxime & Aminoglycosides or Ampicillin 200 mg/Kg/day For 10-14 days. "G-ven"
- 4- **ttt of complications:**
 - Empyema $\Rightarrow$ intercostal tube & drainage under water-seal.
 - HF $\Rightarrow$ Diuretics $\pm$ Digitalis.
 - Respiratory failure $\Rightarrow$ mechanical ventilator.

5- H-influenza vaccine.

Viral pneumonia

- It is considered when the fever is mild or absent & the patient doesn't look seriously ill.
- It is either $\Rightarrow$ Bronchopneumonia or interstitial pneumonia.

RS Viral pneumonia

C/O

- Fever, low grade.
- Cough + sneezing
- Expectoration.
- Dyspnea.
- Grunting.
- **Wheeze**: $\rightarrow$ d.t. neuro irritation $\rightarrow$ $\oplus$ vagal tone $\rightarrow$ BS.
- Chest pain is rare (due to viral myositis or pleurisy)
- Cyanosis (rare).

O/E

❖ Inspection:

- Tachypnea & working alae nasi.
- Intercostal & subcostal retraction.
- Expiratory grunting.
- Cyanosis in severe cases.
- Limitation of movement of the chest bilateral.

❖ Palpation:

- Central trachea.

Palpable wheeze

❖ Percussion:

- Dullness bilateral & patchy, Tender percussion if there is pleurisy.

❖ Auscultation

- Diminished air entry bilateral.
- Bronchial breathing.
- Fine or medium sized consonating crepitations patchy all over the chest. + *Sibilant*
- Bilateral sibilant ronchi all over the chest.

*generalized
Rhonchi + wheezes
BS.*

Complications

1- Pleural effusion:

- rare

2- Respiratory failure:

- It is mainly seen in infants with severe pneumonia
 - $PO_2 < 50$ mmHg.
 - $PCO_2 > 60$ mmHg.
 - $PH < 7.2$.

3- HF:

- Mostly due to viral myocarditis.

4- Paralytic or toxic ileus: rare.

5- post viral autoimmune disease.

Investigations

1- CBC: $\uparrow\uparrow\uparrow$ WBCs mostly lymphocytosis

2- CXR $\Rightarrow$ It is important:

- To identify the pathological type
 - Bronchopneumonia.
 - Interstitial.
- To detect complications as cardiomegaly, pleural effusion

3- Blood gases to evaluate the respiratory function.

4- Others $\Rightarrow$ viral specific antibodies & serologic techniques for virus isolation.

viral isolation, viral markers.



1- Hospitalization

- is needed in cases with marked RD or complications for supportive care
 - O₂ therapy.
 - Fluid intake.
 - Bed rest.

2- Symptomatic ttt

- Fever $\Rightarrow$ Aspirin (is contraindicated ?) but use paracetamol 15
- Expectorant & mucolytics. - Bronchodilator "d + B3"

③- Specific ttt:

- Influenza A : Ribavirin can be used $\rightarrow$ RSV.

4- ttt of complications:

- HF $\Rightarrow$ Diuretics $\pm$ Digitalis 0.01 mg/kg/D. *No empyema
- Respiratory failure $\Rightarrow$ mechanical ventilator.

Mycoplasma pneumonia

Nat
w/p

- Occurs worldwide and is endemic in large communities.
- Peak incidence in school age children "Severely immunosuppressed". Non Bact., Non Viral, non parasite.
- C/P: starts by headache, malaise, fever, rhinorrhea, sore throat, hoarseness & cough then all clinical symptoms & signs of pneumonia.
- High titre of cold Ab $\Rightarrow$ autoimmune hemolytic anemia. تقریباً الوحيدة
- TTT $\Rightarrow$ Erythromycin, Clarithromycin Or azithromycin 15 mg/Kg/day.

Complication :- auto imm. Haemolytic anaemia.

invest. :- Compstest. $\rightarrow$ القیاس بینه ال Cold

37° Warm ال الدرجة

Bronchial asthma

Critical Topic

Definition

- It is a disease characterized by **airway hyper-responsiveness** to **various stimuli** with **spontaneous relieve**:

Epidemiology

- The prevalence has increased in the last 3 decades. It is about **10-15 %** among children.

Risk factors:

1. Poverty. *Repeated Bronchitis*
2. Black races.
3. Maternal age **<20** years at time of birth. *asthma? ... Aching. ← من أكثر عائلات الألم*
4. Maternal smoking.
5. Birth weight **<2.5 Kg**.
6. Overcrowding.
7. Intense **allergenic** exposure in infancy.
8. **Sex**: before **puberty** boys are twice affected more than girls while **after** puberty both are equal. *2:1*

Prognosis

- **50 %** of all asthmatics become **symptom free** within **10-20 years**, recurrence is common in adulthood.
- This occurs in mild & moderate cases, while in severe cases **95%** become **asthmatic adults**.
- Mortality has increased in the last 3 decades especially among **black** races.
- **Age of onset**: **30 %** of patients are symptomatic by **1 year** of age while **80-90 %** are symptomatic **before 5 years**.

Precipitating factors

1. Infections:

- It is the **most important** factor esp. viral infection e.g. **RSV**

2. Drugs:

Aspirin & Endomethacin $\Rightarrow$ cyclo-oxygenase $\Rightarrow$ $\uparrow\uparrow$ SRS-A

3. Food: Milk, egg, fish & nuts.

4. House dust.

5. Pollens.

6. Psychological disturbance

Increase the **severity** of asthma, but **not the cause**, just aggravate.

7. Endocrinal disorders:

In **males**, asthma usually **improve at puberty** while in females it may persist leading to adult asthma $\Rightarrow$ Why?

8. Genetic role

AD gene carried on chromosome **no. 11** $\Rightarrow$ $\uparrow$ T-helper & $\downarrow$ T-suppressor.

$\oplus$ B-lymphocytes



Pollen

Classification

1. Extrinsic (Allergic asthma):

- + Ve family history.
- + Ve skin test.
- High Ig E titre

→ IgE mediated.

2. Intrinsic (non immunologic)

- Viral agents provoke asthma in early life as RSV, Para influenza & influenza viruses.
- IgE normal.
- Skin tests are -Ve

→ Viral mediated

3. Mixed.

Special types

- Exercise-induced asthma.
- Aspirin-induced asthma.
- Nocturnal asthma

GERD → Aspiration.
Normal bronchiole
steroids.

Patho-physiology

Triad of pathophysiology

1) Bronchospasm (1st 6 hrs)

- Histamine
- SRS-A
- Prostaglandin.
- ThromboxanA₂
- Bradykinin.
- PAF.

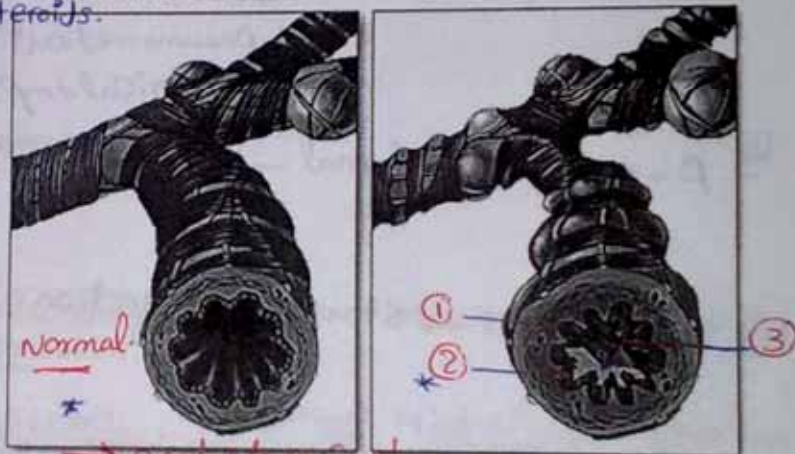
Dry Cough
for timing

2) Mucosal edema (> 6hrs)

As above.

3) Increased mucus secretion

- SRS-A
- Prostaglandin.



⇒ productive cough.

All these factors ⇒ Airway obstruction during expiration ⇒ distal airway trapping ⇒ hyper-inflated chest.

- ❖ Extrinsic asthma: allergens exposure ⇒ induce IgE mediated mast cell degranulation & release chemical mediators.
- ❖ Intrinsic asthma: viral infections ⇒ stimulation of the: parasympathetic mediated vagal reflex causing bronchospasm.

C/P

C/O:

History of repeated attacks of

- 1- Cough & expectoration.
- 2- Dyspnea
- 3- Tachypnea
- 4- Wheezes
- 5- Irritability

On exposure to certain allergen.

Examination:

❖ **Inspection:**

- Tachypnea & working alae nasi.
- Intercostal & subcostal retraction.
- Cyanosis in severe cases.
- Limitation of movement of the chest bilateral.
- Barrel shape chest.

❖ **Palpation**

- Central trachea.
- Palpable wheeze.

❖ **Percussion**

- Bilateral hyper-resonant chest.

❖ **Auscultation**

- Bilateral diminished air entry.
- Harsh vesicular breathing.
- Bilateral sibilant rhonchi & sometimes sonorous rhonchi all over the chest.



Barrel shape chest

Grades

Classified according to: *مقدار الأعراض*

1. Frequency of attacks.
2. Frequency of nocturnal symptoms.
3. FEV1sec.

← mild
moderate
severe

Investigations

1- **CXR:**

- not to diagnose but to exclude other causes of wheezy chest e.g. viral pneumonia, T.B. lymphadenopathy, F.B.

2- **CBC:**

- Eosinophilia (>250-400 cell / mm³). *not present in intrinsic Asthma*
- Leucocytosis if there is underlying infection. *- polycythemia*

3- **Sputum analysis**

- white-tenacious-casts of epithelial bronchioles, mucus, eosinophils.

4- **Allergic skin test:** *sp. invest.*

- results may not be related to the mechanism producing clinical illness, but must be correlated to history & combined with RAST (Radio- Allergo- Sorbant Test) to identify allergens.

5- **↑↑IgE & G4.** → *sp. invest. ↑ in cases of extrinsic asthma*

6- **Blood gases** :to assess the respiratory function.

7- **Pulmonary function tests:**

- * Mild cases: no abnormality.
- * Moderate cases:
 - Functional residual capacity: ↑↑↑
 - Residual volume: ↑↑↑
 - Vital capacity: ↓↓↓
 - Timed vital capacity e.g. forced expiratory volume in one second: ↓↓↓

RAST ← not seen
very expensive
in vitro
Research Pur.

Complications

1. Massive lung collapse if there is complete airway obstruction.
2. Pneumothorax & pneumo-mediastinum or even surgical emphysema, if there is partial obstruction.
3. Emphysema.
4. Cor-pulmonale.
5. Pulmonary infection and later on Bronchiectasis.

FEV₁

5. Pulmonary infection & later on bronchiectasis.



1- TTT of the acute severe attack (status asthmaticus):-

" + Resp. distress "

1. O₂ therapy

- to correct hypoxia, 40-50% O₂ is usually sufficient it should be given continuously & withdrawn gradually.

2. I.V. fluid therapy (2/3 maintenance)

⊕ Complete Rest.

- To provide an adequate fluid intake & to prevent dehydration.
- Liquefy the viscid secretion.

3. Drugs:

A) Sympathomimetics:

a) Epinephrine 0.01 mg/kg/dose S.C.

follow up pulse, B.P., Pr...

- It can be repeated every 20 min for maximum 2 doses side if there is no tachycardia & hypertension.

improve ald., Sec., B.S.

b) B₂-agonists: e.g.:α in cap. B₂

- Terbutaline "Bricanyl"
- Sulbutamol "Ventolin"
- Fenoterol "Berotec"

- All these drugs can be nebulized using a special apparatus "Nebulizer"

- Mechanism of action → activation of adenyly cyclase
⇒ ↑↑ intracellular C-AMP
⇒ relaxation of the bronchial ms.

Dose:

- Sulbutamol 0.6 mg/kg/D 6 hourly.
- Terbutaline 0.3 mg/kg/D 6-8 hourly.



B) Theophylline:

- If there's no response to Sympathomimetics
- Mechanism of action: suppression of phospho-diesterase enzyme
⇒ ↑↑ C-AMP.
- Dose initial = if there's no aminophylline intake in the last 24 hrs = 5mg/kg over 20-30 min. The maintenance dose 20 mg/kg/ 24hr IV drip.

C) Anti-cholinergic drugs: inhaler form.

D) Corticosteroids: → دكتور مصطفى العبد

in Resistant Cases. Given in severe cases as methyl Prednisolone 1 mg / kg / 6 hrs in the 1st 48 hrs, followed by 1 mg/kg/D

E) Antibiotics:

- If there is superimposed bacterial infection.

4. Correction of acidosis ⇒ NaHCO₃.

5. TTT of HF if presents Digitalis 0.01 mg/kg D.

6. Mechanical ventilation ⇒ if there's respiratory failure.

في بعض
الحالات

2- TTT in between the attacks:A. General: -

1. Avoid exposure to non specific irritants as : tobacco smoke, fumes, irritants sprays etc.
2. Avoid exposure to precipitating factors.
3. Emotional support.
4. Proper ttt of respiratory infection.
5. Long term controllers:

① Long acting beta 2 agonists by inhalation.

▪ Slow release Theophylline oral RD.

▪ One of mast cell stabilizing drugs.

8. Steroids: 1-2 mg / kg / day to be discontinued within 7 days (inhaled)

▪ Steroids better used in children (over 7 years).

B. Mast cell stabilizing drugs:1. Ketotifen "Zaditin":

- Orally 0.5-1 mg twice daily.

- Mechanism of action: -

- Release of chemical mediators.

- Ca influx.

- Antihistaminic, anti-kinins & anti-leukotriens.

2. Disodium cromoglycate "Intal"

- Used by inhalation actions:

- As above + Mast cell stabilizer.

Bronchiectasis

Definition

Irreversible abnormal dilatation of the bronchi.

Etiology

A. Congenital type:

1- Isolated or.

2- As part of kartagener syndrome:

- Congenital bronchiectasis.
- Dextro-cardia.
- Absent frontal air sinuses or frontal sinusitis.

B. Acquired type:

It may be due to either:

1- Obstruction or.

2- Infection & fibrosis.

* Bronchial obstruction

It may be either:

- a. complete or → absorption collapse → ↑ -ve Dr.
- b. Partial.

* Bronchial obstruction may be due:

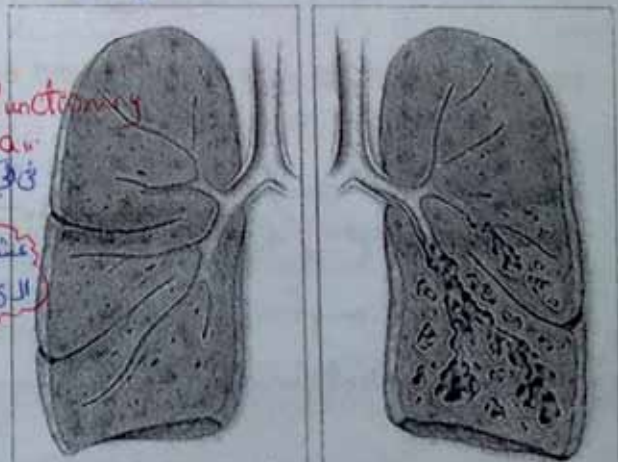
1- In the lumen

- F.B.
- Thick secretion.

2- In the wall

- TB granuloma. TB adenoma.
- Bronchostenosis.

3- Pressure from outside: by LN or Tumor.



any Bronchiectasis:-

• Bilat. lower lobe

But if Congenital, it may differ.

CIP

min 50 Tab 8

A. Symptoms:

1) Suppurative syndrome:

- Cough - with excessive purulent fetid sputum more in the morning & increase on stooping forwards. *→ أصعب عطلة .. عطلة الصبح **
- The onset is usually gradual, the course is progressive over years with characteristic winter exacerbation.

yellowish, greenish.

دكي التي يتحول
التي2) Hemoptysis:

- Usually blood tinged sputum, but frank Hemoptysis may occur.

It may be the only presenting symptom in?

isolated Bronch
in upper lobe

- 3) Chest pain ⇨ Why?
- 4) Anorexia & poor weight gain.
- 5) Fever.

Bronchiect. Hygic. sicc. إلى في الباطنة

B. Signs:

1- General signs

- 1. Low grade fever & wt loss.
- 2. Puffy eyelids ⇨ Why?
- 3. Clubbing of the fingers & may be osteoarthropathy.
- 4. Edema of L.L. ⇨ Why?

Chronic
Toxaemia2- Chest signs:❖ Inspection:

- Mild RD.
- Limitation of movement of the chest especially in to basal parts.
- Retraction in the basal parts & bulge in apical parts.

❖ Palpation:

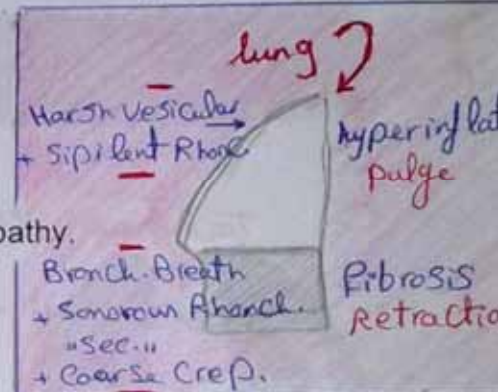
- Central trachea.
- May be palpable wheeze in the apical parts.

❖ Percussion:

- Patchy of dullness in the basal parts & may be hyper-resonant note in the apical parts.

❖ Auscultation

- Diminished air entry.
- Patchy areas of bronchial breathing & medium sized consonating crepitations, sonorous ronchi & coarse crepitations if there is lung secretions on the basal parts.
- Sibilant ronchi on the apical part.

نسمع فيها
الأصوات

Investigations

1- Sputum culture & sensitivity2- CXR:

- Honey-comb appearance in basal parts & may be emphysema in upper parts.
- Consolidation may be seen around bronchiectatic zones.

3- Bronchography: This is useful to

- Confirm the diagnosis.
- Localize the site.

4- Bronchoscope:

- May reveal the cause.
- May be used to aspirate pus or instillation antibiotics.

* CBC :- neutrophilia d.t 2ry Bact. inf.

صبيحة
واحدةResp. في
So ABG في

Therapeutic

5- **Pulmonary function tests:**

- reveals increased pulmonary resistance residual volume.

6- **Electron microscopic examination**

- of materials from nasal & bronchial mucosal biopsy to diagnose immotile cilia syndrome.

Treatment

1. Postural drainage of pus. *يقدر في وضع السجود وحده يطيب له فخره - تنكر قد ما فخر*
2. Antibiotics according to culture & sensitivity
3. Bronchoscopic aspiration & antibiotics instillation.
4. Symptomatic Mucolytic & Expectorant. *+ Bronchodilator.*
5. Surgery (indications):
 - Presence of serious symptoms e.g. Hemoptysis.
 - Infection not responding to repeated medical ttt.
 - Localized lesion.

Acute dry pleurisy

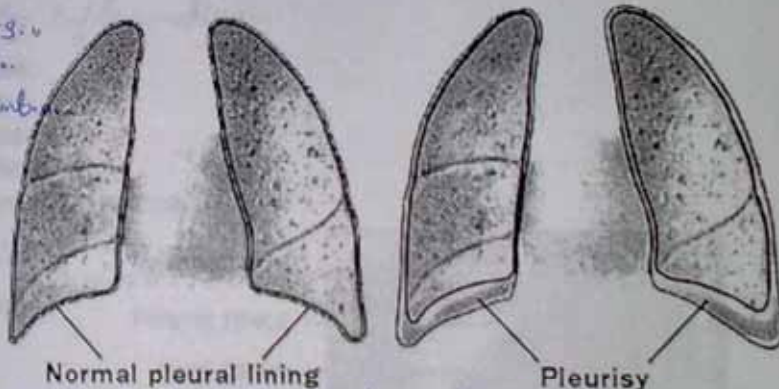
Etiology

A. **Primary pleural affection:**

- 1) T.B.
- 2) Rheumatic. *Collagen dis.*
- 3) Viral. *e.g. Common Cold.*
- 4) Uremia. *acc. on Serous membrane*
- 5) Malignant (rare)

B. **2ry to:**

- 1) **Lung disease:**
 - Pneumonia.
 - Lung abscess.
 - T.B.
 - **Infarction.**
- 2) **Mediastinal disease:**
 - Mediastinitis. *dt. Per. of oes. e.g. sharp body swallowing.*
 - Pericarditis.
- 3) **Chest wall disease:**
 - Osteomyelitis.
 - Fracture rib.
- 4) **Sub diaphragmatic** disease sub-diaphragmatic & amoebic liver abscess.



C/P

A. **Symptoms:**

- 1- Chest pain, stitchy in character, increasing with cough & Straining
- 2- Dry cough. *irritative cough.*
- 3- Dyspnea *⇒ Why? Tachypnea.*
- 4- General symptoms as fever, headache & malaise.

B. **Signs:**

- 1- **Inspection** : limitation of movement on the affected side.
- 2- **Palpation** : Pleural rub.
- 3- **Percussion** : Tender
- 4- **Auscultation** : Pleural rub. *Friction Rub.*

Investigations

- 1- **CXR**: to detect the underlying chest disease.
- 2- **Other investigations** to detect the cause e.g.
 - Tuberculin test.
 - Urea & creatinine.
 - Abdominal sonar.

Treatment

- 1- ttt of the cause.
- 2- Analgesics to relief pain. → endomethacin → severe gastritis

Pleural effusion

Definition

Collection of fluid in the pleural sac.

Classification

A. **Serous**: which may be:

I. **Exudate**:

- Idiopathic ⇨
- 2ry to ⇨ "near by inflammation".
 - 1- Pleural disease.
 - 2- Lung disease;
 - 3- Chest wall disease.
 - 4- Mediastinal disease.
 - 5- Infradiaphragmatic disease.

II. **Transudate**: → Always Bilat.

- 1- HF.
- 2- Nephrotic syndrome.
- 3- Liver cirrhosis.

B. **Hemorrhagic**:

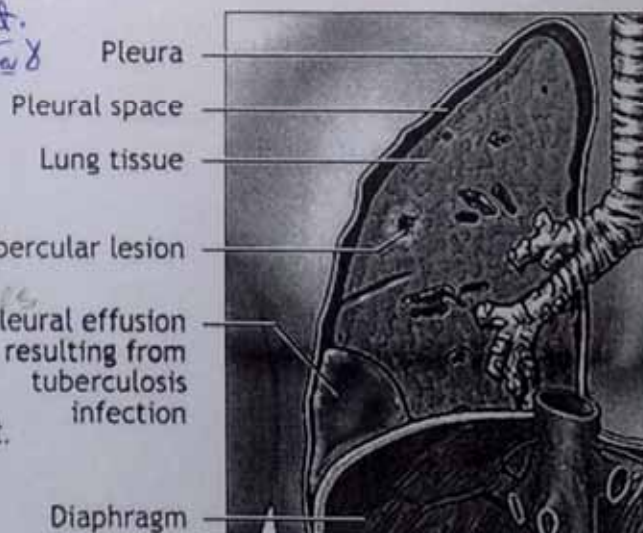
- T.B.
- Klebsiella pneumonia.
- Traumatic.
- Malignancy.

C. **Chylous**:

- Thoracic duct obstruction.
- Traumatic injury to thoracic duct.

D. **Empyema**:

- Pneumonia. , Bronchiectasis.
- Rupture of lung abscess.
- Contamination during tube introduction.
- Rupture of sub-diaphragmatic abscess.



C/P

A. **Symptoms**:

- 1- High fever & toxemia esp. with empyema.
- 2- Irritative cough.
- 3- Dyspnea.
- 4- Cyanosis in massive effusion.
- 5- Symptoms related to etiology.

① manifest of under lying pathology.

B. signs:

- ❖ **Inspection:**
 - RD
 - Limitation of movement on the affected side.
 - Bulge $\Rightarrow$ unilateral. *(Common)*
- ❖ **Palpation:**
 - The trachea is pushed to the opposite side in massive effusion.
 - $\downarrow\downarrow$ TVF
- ❖ **Percussion:**
 - **Stony dullness** on the affected side.
- ❖ **Auscultation:**
 - air-entry.
 - Breath sounds & adventitious sounds depends on the underlying etiology.

Ret. $\rightarrow$ underlying Collapse or Fibrosis

Investigations

- 1- **CXR**
 - Diffuse homogenous opacity obliterating the costophrenic angle, trachea pushed to opposite side.
- 2- **Pleural aspiration for:** *color, sp. gravity*
 - Physical examination *18 mins at last*
 - Chemical.
 - Bacteriological.
 - Cytology.
- 3- **Pleural biopsy.** *if malignancy is suspected.*
- 4- **Tuberculin test.**
- 5- **Sputum examination For T.B.**



4 tubes

see clinical

4 tubes

Complications

1. **With staph**
 - Bronchopleural fistula.
 - Pyopneumothorax.
2. **Local**
 - Pericarditis.
 - Pulmonary abscess.
 - Peritonitis.
 - Osteomyelitis of ribs.
3. **Septic**
 - Meningitis.
 - Arthritis.

How to differentiate bet. transudate & exudate.

Treatment

1. Of the underlying cause.
2. Symptomatic.
3. Tube drainage under-water seal, the tube inserted for 7-10 days.
 - *pus even if small amount*
 - *massive eff. $\rightarrow$ Regardless type*
 - *marked by cyanosed, distressed*
 - *Percussion, X-Ray eff. Reach 2nd space.*

HEMATOLOGY COMPONENTS OF THE BLOOD

Whole Blood



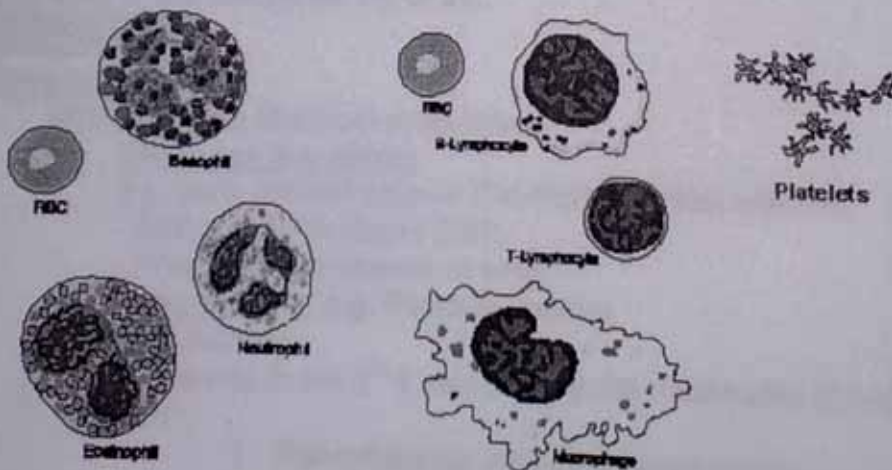
- ☐ Plasma
- ☐ White Blood Cells
6-9000/mm³
- ☐ Platelets
200-400,000/mm³
- ☒ Red Blood Cells
4-5 Million/mm³

Hematocrit (Packed Cell Volume)



- Plasma
- Buffy Coat
(WBC & Platelets)
- RBC's
36% - 54%

Blood Cells



Hematology

Anemia

Definition

It is a decrease of Hb % below 11 gm % regardless the age or sex.

Causes

1. Impaired cell synthesis.
2. Hemorrhage.
3. Hemolysis.

Impaired RBCs synthesis

Deficiency of BM Requirement

States originate from decreased intake, increased losses & demand.

1. **Iron deficiency anemia** → Microcytic hypochromic anemia.
2. **B12 & Folic acid deficiency** → Megaloblastic anemia.
3. **B6 deficiency** → Sideroblastic anemia.
4. **Protein deficiency** → Any type of anemia.
5. **Copper deficiency** → Microcytic hypochromic anemia.
6. **Vitamin E deficiency** → Hemolytic anemia.
7. **Vitamin A deficiency** → Microcytic anemia
8. **Vitamin B1** → Hypoplastic anemia.

BM failure

Due to hypoplasia of the BM either 1ry or 2ry.

Primary BM failure

1. Heredofamilial:

With defective stem cell precursors

a. Single cell line defect:

- e.g. pure red cell aplasia (Diamond blackfan anemia)
- Autosomal recessive (AR)
 - Presents with anemia at birth.

b. Pancytopenia: e.g. Fanconi anemia

- AR disease.
- Presents in the 1st 4 years of life not necessary at birth.
- C/P:

1. Pancytopenia without splenomegaly.

2. Somatic changes:

- Short stature.
- Thumb & radius anomalies.
- Microcephaly.
- Renal defects.

3. Café au lait patches: the skin stains deeply with excess hemosiderin deposition 2ry to ineffective erythropoiesis

- Treatment:

1. BM stimulants: e.g. steroids & anabolics.
2. BM transplantation.

Pediatrics

2

Hematology

II. Idiopathic:

- Mostly due to immunologic process.
- Treatment:
 1. Immunosuppressant.
 2. BM stimulants: e.g. steroids & anabolics.
 3. BM transplantation

Secondary BM failure

- I. Toxins: infection & septicemia.
- II. Drugs: Chloramphenicol, sulfonamides & cytotoxic.
- III. Irradiation:
- IV. Infections: Human parvo virus, Hepatitis B virus & Epstein bar virus.

Dyshemopoietic

1. Infiltration of the BM by malignant or non malignant cells.
2. Try to systemic diseases: endocrinal, hepatic, renal

Iron Deficiency Anemia

Daily requirement of iron: - 2-3 mg / Kg / Day.

Etiology

I. Decrease intake:

1. Infants on cow milk or unfortified artificial milk.....why?.
2. Delayed weaning.why?.

II. Decrease absorption:

1. Chronic diarrhea.
2. Malabsorption syndrome.
3. Excess tea, phytate, oxalate & anti-acids.

III. Excess loss:

Due to chronic blood loss e.g. epistaxis, hemoptysis, hematemesis, ankylostoma, ulcerative colitis & cow milk protein allergy.

IV. Decrease stores:

1. Premature.
2. Low birth weight.

V. Excess requirement:

1. Growing children.
2. Adolescent.

Clinical Picture

1. General manifestations of anemia:

- a. Lack of concentration & decrease performance.
- b. Dizziness.
- c. Headache.
- d. Syncopal attack.
- e. Anginal pain.
- f. Muscle cramps & weakness.

2. Red glazed tongue.

3. Koilonychia.

4. Anorexia & pica.

5. Mild splenic enlargement in 10-15 % of cases.



Hematology

Investigations**I. For diagnosis of iron deficiency anemia:**

1. CBC:

- Microcytic hypochromic anemia.
- Low reticulocytic count or even zero.
- No abnormal cells in blood film.

2. Low serum iron ($< 30 \text{ ug / dl}$) & serum ferritin.3. High serum iron binding capacity ($> 350 \text{ ug / dl}$).

4. Increased free erythrocyte protoporphyrin.

II. For diagnosis of the underlying etiology:

1. Stool analysis.....for ankylostoma ova.

2. Occult blood in the stool.

D.D**From other causes of microcytic hypochromic anemia:**

1. Chronic lead poisoning.

2. Thalassemia.

3. Sideroblastic anemia.

Treatment**I. Prophylactic ttt**

1. Adequate iron intake for pregnant females

2. Early & proper weaning.

3. Prophylactic iron supplementation after the 3rd month in premature & low birth weight**II. TTT of the underlying cause**

1. TTT of ankylostoma.

2. TTT of any bleeding focus.

III. Iron therapy**1. Oral :**

a. Liquid ferrous fumarate (45mg) .

b. Tablet ferrous sulfate (60mg) & ferrous gluconate (35mg).

Dose: 6 mg / kg / day elemental iron.

Duration of therapy : 4-6 weeks after correction of anemia.

Side effects: GIT irritation.

Dark stool.

2. Parenteral iron :

a. Fe dextran (100mg).

b. Fe sorbitol (100mg).

The hematological response becomes evident after 48-72 hrs in the form reticulocytosis

VI. Packed RBCs transfusion1. Sever anemia ($\text{Hb} < 6 \text{ gm \%}$).

2. Anemic HF.

3. Surgical emergency.

Megaloblastic anemia

Etiology

It is caused by B12 or folic acid deficiency.

Causes of B12 deficiency

I. Decrease intake:

Very rare as in severe conditions of malnutrition.

II. Decrease intrinsic factor :

1. Partial or total gastrectomy.
2. Pernicious anemia either juvenile or adult type.

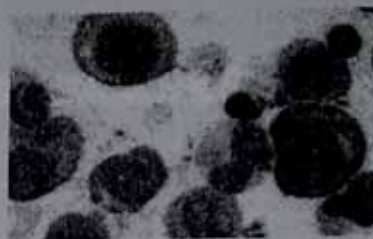
III. Consumption of B12 in the intestine:

1. Diphylobothrium latum.
2. Over-growth of bacteria e.g. in blind loop syndrome.

IV. Decrease absorption:

1. Crohns disease.
2. Resection of the terminal ileum.

V. Decrease stores: Advanced liver disease.



Causes of folic acid deficiency

I. Decrease intake:

Very rare as severe conditions of malnutrition & infants on goat milk.

II. Decrease absorption:

Chronic diarrhea & malabsorption syndrome.

III. Consumption of folic acid due to increase requirement:

Chronic hemolytic anemia.

IV. Drugs:

-Sulfonamides. -Methotrexate.

Clinical picture

1. Manifestations of pancytopenia:

- a. General manifestations of anemia.
- b. Repeated infections.
- c. Bleeding tendency.

2. GIT manifestations :

- a. Recurrent glossitis.
- b. Chronic diarrhea.
- c. Failure to thrive.

3. Neurological manifestations (in B12 deficiency only):

Sub acute combined degeneration of the cord

- a. Peripheral neuritis.
- b. Pyramidal tract affection.
- c. Posterior column affection.

Investigations

I. CBC:

- Macrocytic normochromic anemia.
- Leucopenia (hyper segmented WBCs).
- Thrombocytopenia & Immature platelets.

II. BM aspirate: Megaloblastic changes

III. Serum folate & B12 assay

IV. Schilling test.

V. FIGlu test

VI. Detection of antibodies against the parietal cells of the stomach.

Pediatrics

5

Hematology

Treatment

1. B12 injection 250 mg / 4-8 weeks.
2. Oral folic acid 5 mg / day.

Hemolytic Anemia

Definition

- Anemia due to short life span of RBCs.

Etiology

- Destruction of RBCs due to :
 - A. Corpuscular defect.
 - B. Extra-corpuscular defect.

Corpuscular Defects**I. Acquired:**

Malaria infection.

II. Congenital or hereditary:**A. Cell wall defects:**

1. Spherocytosis.
2. Elliptocytosis.
3. Ovalocytosis.

B. Enzymatic defects:

1. Glucose-6-phosphate dehydrogenase deficiency.
2. Pyruvate kinase deficiency.

C. Abnormal Hb:

1. Quantitative defect → thalassemias.
2. Qualitative defect → sickle cell disease.

**Extra-Corpuscular defects****I. Non - immune:**

Infection & DIC.

II. Immune:**A. Iso-immune:**

Rh & ABO-incompatibility

B. Auto-immune:

1. SLE.
2. Idiopathic.

Approach to Diagnosis

Approach to diagnosis should include:

1. The C/P suggesting hemolytic disease.
2. The laboratory finding suggesting hemolytic disease.
3. Determination of the underlying cause by special investigations.

Clinical Picture

According to the C/P, hemolytic anemia is classified into 2 types:

- A. Chronic hemolytic anemia (CHA):** in which hemolysis occurs extra-vascular.
- B. Acute hemolytic anemia (AHA):** in which hemolysis occurs intra-vascular.

Chronic Hemolytic Anemia

Ethnic factors

- Black race → Sickle cell anemia.
- Mediterranean → Thalassemia.

General Clinical picture

- Anemia : not responding to hematinics.
- History of frequent blood transfusion.
- Tinge of jaundice.
- Hepato-splenomegaly: due to:
 - Extra-medullary hemolysis.
 - Extra-medullary hemopoiesis.
 - Hemosiderosis.
 - Intercurrent infection.
- Dark colored stool: due to increased oxidized stercobilinogen.
- Normal colored urine.
- Mongoloid facies : Due to hyperactive BM (in long standing cases).
- Finally can be presented by one of the complications (see later) .
- Positive family history in hereditary causes.

General complications

- Complications of frequent blood transfusion: HBV, HCV & HIV
- Traumatic rupture spleen.
- Hypersplenism.
- Hemosiderosis:
 - Dark colored skin.
 - Cardiomyopathy.
 - HSM.
 - Diabetes mellitus.
 - Peripheral neuropathy.
 - Hypo-endocrinal functions.
 - Leg ulcers.
- Gall stones.
- Heart failure: due to :
 - Anemia.
 - Hemosiderosis.
- Repeated infections: due to :
 - Decrease WBCs if there is :
 - 1) Hypersplenism.
 - 2) Megaloblastic crises.
 - 3) Hypoplastic crises.
 - HF → Repeated chest infection.
 - Decrease tufts in after splenectomy.
- Stunted growth: due to:
 - Anemia → Tissue hypoxia.
 - Hemosiderosis → Hypo-endocrinal functions.
 - Repeated infections.
 - Repeated pathological fracture.

Pediatrics

Hematology

- Pathological fracture: due to hyperactive BM.
- Crises:
 - Megaloblastic crises due to folic acid deficiency.
 - Hypoplastic crises → Idiopathic or post viral.
 - Hemolytic crises.
 - Hyper-hemolytic crises if associated with acute hemolytic anemia.

Investigations

I. For diagnosis of chronic hemolytic anemia:

1. CBC:

- All causes of CHA lead to normocytic normochromic anemia except thalassemia → microcytic hypochromic anemia.
- Increased reticulocytic count
- Abnormal cells can be seen in blood film :
 - Spherocytes → Spherocytosis.
 - Sickle shape → Sickle cell anemia.
 - Target cells & anisocytosis → Thalassemia.

2. Increased serum iron.

3. Low serum iron binding capacity.

4. Increased indirect bilirubin.

5. Stool analysis → Increased stercobilinogen.

6. Urine analysis → Increased urobilinogen.

7. Radiological findings:

- Long bones: - Thin cortex & wide medulla (mosaic pattern).
- Skull :-Wide deploic space (hair on end appearance).

II. For diagnosis of the underlying etiology:

1. Osmotic fragility test → Spherocytosis.

2. Sickling test → Sickle cell anemia.

3. Hb-electrophoresis:

- Increased Hb-F → Beta-thalassemia major.
- Increased Hb-A2 → Beta-thalassemia minor.
- Hb-S → Sickle cell anemia.

4. Alkali denaturation for Hb F in Beta-thalassemia.

5. Acidified serum lyses test (Ham's test) for paroxysmal nocturnal hemoglobinuria (PNH).

N.B. The diagnostic investigation for hemolytic anemia is decreased red cell survival studies 51 Cr.

Treatment

I. Packed RBCs transfusion:

1. Ordinary transfusion: Packed RBCs transfusion are given only when Hb% < 6 gm %
2. Hyper - transfusion: Packed RBCs transfusion are given only when Hb% < 10 gm %
3. Super - transfusion: Packed RBCs transfusion are given only when Hb% < 12 gm %

II. Folic acid: 1-5 mg / day.

Pediatrics

Hematology

III. Iron chelating therapy (usually after the age of 5 years):

1. Oral (under trial)

2. Parenteral:

Desferrioxamine by continuous S.C infusion using portable pump
dose 25 – 40 mg / kg / day.

VI. TTT of complications

Hereditary spherocytosis

Etiology

- Autosomal dominant (AD), in which there is abnormal spectrin in the cell membrane of the RBCs lead to Na influx & water inside the RBCs which lead to deformity of the RBCs , sequestration & destruction in the spleen.
- 10-20 % of cases have no family history.....why?

Clinical Picture

➤ **Age of onset:** can be presented since birth by neonatal jaundice.

- Anemia
- History of frequent blood transfusion.
- Tinge of jaundice.
- Hepato-splenomegaly
- Dark colored stool.
- Normal colored urine.
- Mongoloid facies
- Finally can be presented by one of the complications.

General complications

- Complications of frequent blood transfusion: HBV, HCV & HIV
- Traumatic rupture spleen.
- Hypersplenism.
- Hemosiderosis.
- **Gall stones (common).**
- Heart failure.
- Repeated infections
- Stunted growth.
- Pathological fracture.
- Crises.
- **Complications of neonatal jaundice.**



Investigations

I. For diagnosis of chronic hemolytic anemia

1. CBC:

- Normocytic normochromic anemia.
- Increased reticulocytic count
- Blood film : Spherocytes & polychromesla.

2. Increased serum iron .

3. Low serum iron binding capacity .

4. Increased indirect bilirubin.

5. Stool analysis → Increased stercobilinogen.

6. Urine analysis → Increased urobilinogen.

Hematology

7. Radiological findings:

- Long bones: - Thin cortex & wide medulla (mosaic pattern).
- Skull: Wide deplcic space (hair on end appearance).

II. Diagnostic investigations

1. Osmotic fragility test: Spherocytes lyses in higher concentration of saline than normal RBCs.
2. Autohemolysis at 24-48 hrs corrected by addition of glucose.

Treatment

1. Packed RBCs transfusion:
2. Folic acid: 1-5 mg / day.
3. Iron chelating therapy usually start after the age of 5 years.
4. TTT of complications:
 - Gall stones : Cholecystectomy.
 - Splenectomy for moderate to severe cases.

Thalassemia

Definition

Quantitative Hb defects

Etiology

Autosomal recessive (AR), in which there is mutation in the globins genes that reduce or totally abolish synthesis of one or more of the globins chains.

1. α -Thalassemia: Reduced or absent α -globins synthesis.
2. β -Thalassemia: Reduced or absent β -globins synthesis.
3. Hereditary persistence of fetal Hb: Synthesis of elevated amount of fetal Hb persists to adult life without causing clinical disease.
4. $\delta \beta$ Thalassemia: both δ and β -globins chains are reduced or absent.

 β -Thalassemia

- Genes of β -globins are present on chromosome 11.
- Patients are either heterozygous (β - Thalassemia trait) or homozygous (β - Thalassemia intermedia or β - Thalssemia major).
- β -Thalassemia major differs from β -Thalassemia intermedia being more severe & require more frequent blood transfusion.

Patho-physiology

- Reduced or absent β -globin synthesis prevents adequate Hb accumulation in tetramers. So that cells are hypochromic & microcytic.
- Free α -globin chains, instead accumulate & precipitate during early erythroblast development because α -chains are so insoluble.
- α -Chains are highly toxic to erythroblasts causing intra-medullary hemolysis (ineffective erythropoiesis).
- Some of these cells which pass to the peripheral circulation are deformed cells & have short life span (due to destruction in the spleen).



Hematology

C/P

Age of onset: after the age of 6 months.

- Anemia
- History of frequent blood transfusion.
- Tinge of jaundice.
- Hepato-splenomegaly
- Dark colored stool.
- Normal colored urine.
- Mongoloid facies
- Finally can be presented by one of the complications.

Complications

- Complications of frequent blood transfusion: HBV, HCV & HIV
- Traumatic rupture spleen.
- Hypersplenism.
- Hemosiderosis.
- Gall stones.
- Heart failure.
- Repeated infections
- Pathological fracture.
- Stunted growth.
- Crises.

Investigations**I. For diagnosis of chronic hemolytic anemia:****1. CBC:**

- Microcytic hypochromic anemia.
- Increased reticulocytic count
- Blood film : target cells & anisocytosis.

2. Increased serum iron.**3. Low serum iron binding capacity.****4. Increased indirect bilirubin.****5. Stool analysis** → Increased stercobilinogen.**6. Urine analysis** → Increased urobilinogen.**7. Radiological findings:**

- Long bones: - Thin cortex & wide medulla (mosaic pattern).
- Skull: Wide deplcic space (hair on end appearance).

II. Diagnostic investigations:**1. Hb-electrophoresis:**

- Increased Hb-F → Beta-thalassemia major.
- Increased Hb-A2 → Beta-thalassemia minor.

2. Alkaline denaturation test.**III. Anti-natal diagnosis:** By using amniotic fluid or chorionic villous sample.**Treatment****1. Packed RBCs transfusion:****2. Folic acid:** 1-5 mg / day.**3. Iron chelating therapy** usually start after the age of 5 years.**4. TTT of complications:**

1. Gall stones : Cholecystectomy.
2. Splenectomy for hypersplenism.

Hematology

3. Digitalis & diuretics if there's HF.

V. Recent lines of ttt :

1. Neocyte transfusion from single donor.
2. Switch on of the gamma genes by butyrate.
3. Gene therapy.
4. Bone marrow transplantation may provide cure if done early before rise of serum ferritin & liver damage.

α -Thalassemia

- 4 Genes of α -globin are present on chromosome 16.
- Deletion of one, two, three or four loci result in different types of α -thalassemia.

Types

1. One gene defect $\rightarrow$ Carrier.
2. Two gene defect $\rightarrow$ Mild hemolytic anemia.
3. Three gene defect $\rightarrow$ Hb-H disease (4β) $\rightarrow$ mild to moderate hemolysis.
4. Four gene defect $\rightarrow$ Hb-Barts (4γ) $\rightarrow$ hydrops fetalis.

Sickle cell anemia

Genetics & pathophysiology

- o Autosomal recessive (AR), results from a point of mutation that changes the amino acid at position 6 on the β globin chain from glutamic acid to valine (Hb-S).
- o Hb-S behaves normally in the oxygenated state, but polymerize on exposure to hypoxia $\rightarrow$ sickling of RBCs.
- o Sick cells are dehydrated, stiff & have shortened life span because they are destructed in the spleen.

Factors that increase sickling :

- a. Low O₂ tension.
- b. Hyperosmolality.
- c. Fever.
- d. Dehydration.

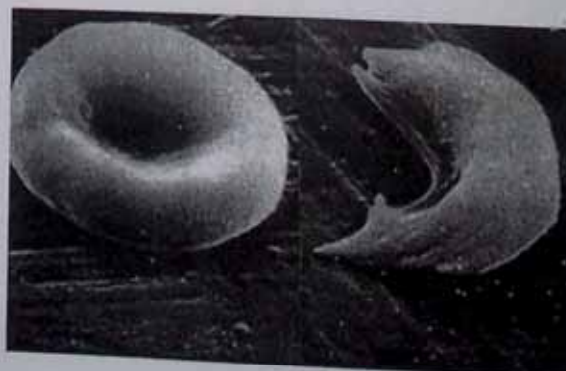
Clinical picture

Age of onset: after the age of 6 months.

Race: Black races are more susceptible.

May present by one of the following crises:

1. Vaso-occlusive crises:
 - Ischemic pain in both hands & foot (Hand foot syndrome).
 - CNS infarction with neurological sequelae.
 - Pulmonary infarction.
 - Splenic infarction (Auto-splenectomy).
 - Sudden blindness.
 - Abdominal angina.
 - Myocardial infarction.
 - Renal infarction.
 - Priapism.



Hematology

2. Hyper hemolytic crises:

- When associated with G-6-PD deficiency.
- Clinically presented with life threatening anemia requiring immediate blood transfusion associated with hemoglobinuria.
- CBC: anemia with high reticulocytic count.

3. Aplastic crises:

- Usually due to infection with parvovirus B19.
- Clinically presented with life threatening anemia requiring immediate blood transfusion.
- CBC: anemia or pancytopenia with low reticulocytic count.

4. Sequestration crises:

- It is due to obstruction of venous return of the spleen → acute massive splenomegaly + shock + collapse.

Investigations

I. CBC: - Normocytic normochromic anemia.

- Increased reticulocytic count
- Blood film : Sickle shape RBCs.

II. Diagnostic investigations:

1. Sickling test : By addition of the reducing agent (Na-metabisulfite).

2. Hb-electrophoresis: ↑↑↑ Hb-S.

III. Antenatal diagnosis: As thalassemia.

Treatment

I. Vaso-occlusive crises:

- Correction of precipitating factors.
- Adequate hydration.
- Analgesics
- O2 therapy.
- Exchange transfusion is recommended in the management of life threatening conditions as acute chest pain, cerebral strokes or retinal lesions.

II. Sequestration crises:

- Exchange transfusion.
- Urgent splenectomy in severe conditions.

III. Hyper hemolytic crises:

- Blood transfusion.

VI. Aplastic crises:

- Blood transfusion.

V. Additional measures:

1. Folic acid.
2. Routine vaccination against capsulated organisms.
3. Anti-sickling agents:

- Hydroxyurea.
- Erythropoietin.
- Butyrate compound.

4. B.M. transplantation: under trial.

G-6-PD deficiency

Etiology

- X-linked recessive.
- On exposure to oxidizing agents → damage of RBCs.
- Fully expressed in hemizygous male & homozygous female.
- Genetic variants:
 1. Type A⁺ → normal variant in blacks.
 2. Type B⁺ → commonest normal variant.
 3. Type A⁻ → Genetic variant associated with deficiencies in blacks.
 4. Type B⁻ → Mediterranean deficiencies in white races.

Clinical picture

Age of onset: can be presented since birth by neonatal jaundice.

1. History of exposure to oxidizing agents:

- Drugs: Antipyretics except paracetamole, Sulfonamides, Anti-malarial drugs, Chloramphenicol.
- Naphthalene.
- Fava-beans → favism.
- Infections.

2. Sever pallor.

3. Jaundice.

4. Red colored urine due to Hb-uria.

5. Loin pain.

Complications

1. Acute tubular necrosis → acute renal failure.
2. Complications of blood transfusion: HBV, HCV & HIV
3. Anemic heart failure.

Investigations

I. For diagnosis of acute hemolytic anemia:

1. CBC:

- Normocytic normochromic anemia.
- Very high reticulocytic count

2. Increased indirect bilirubin.

3. Decreased haptoglobin & hemopexin.

4. Urine analysis → Hb-uria.

II. Diagnostic investigations:

G-6-PD assay.

Treatment

1. Avoiding of exposure to oxidizing agent.
2. Treatment of infection.
3. Blood transfusion in critically low Hb < 6 gm %.
4. Mannitol or lasix → ↑↑↑ urine flow → prevent tubular necrosis due to Hb-uria.

Bleeding disorders

When to suspect bleeding disorders

- Repeated spontaneous heavy bleeding.
- Bleeding from more than one orifice.
- Prolonged bleeding after minor trauma.
- Petechiae, purpura or ecchymosis.
- Bleeding after circumcision, tooth extraction & repeated hemoarthrosis.

Causes of bleeding disorders

1. Vascular disorders.
2. Platelet disorders:
 - a. Thrombocytopenia.
 - b. Thrombasthenia.
3. Coagulation factors defects either inherited or acquired.

Purpura

Etiology

1. Vascular disorders.
2. Platelet disorders:
 - a. Thrombocytopenia.
 - b. Thrombasthenia.

Vascular disorders

1. Allergic: Henoch-Schonlein purpura (HSP).
2. Vitamin C deficiency.
3. Septicemia: Meningococcal septicemia.
4. Collagen diseases: SLE.
5. Steroid induced or associated with Cushing's syndrome due to defective vascular supportive tissue.

Platelet disorders

I. Thrombocytopenia:

Either due to decreased production or excess destruction.

A. Decreased production:

1. Congenital defects:

- TAR syndrome.
- Fanconi anemia.

2. Suppression of BM by:

- Toxins: infection & septicemia.
- Drugs: Chloramphenicol, sulfonamides & cytotoxic.
- Irradiation.

Pediatrics

Hematology

3. Direct invasion of the BM by organisms:

- Human parvo virus.
- Hepatitis B virus.
- Epstein bar virus.

4. Infiltration of the BM by :

- Malignant cells e.g. leukemia or lymphoma.
- Inborn errors of metabolism (IEM).

B. Excess destruction

1. Immune

- ITP.
- Evan \$.
- SLE.
- Transplacental Abs.....neonatal thrombocytopenia.
- Post-transfusion (Antibodies against P- antigen).

2. Non-immune:

- DIC.
- Hemolytic Uremic \$.
- Thrombotic thrombocytopenic purpura.
- Hyper-splenism
- Kasabach Merritt \$ (Giant hemangioma).

II. Thrombasthenia

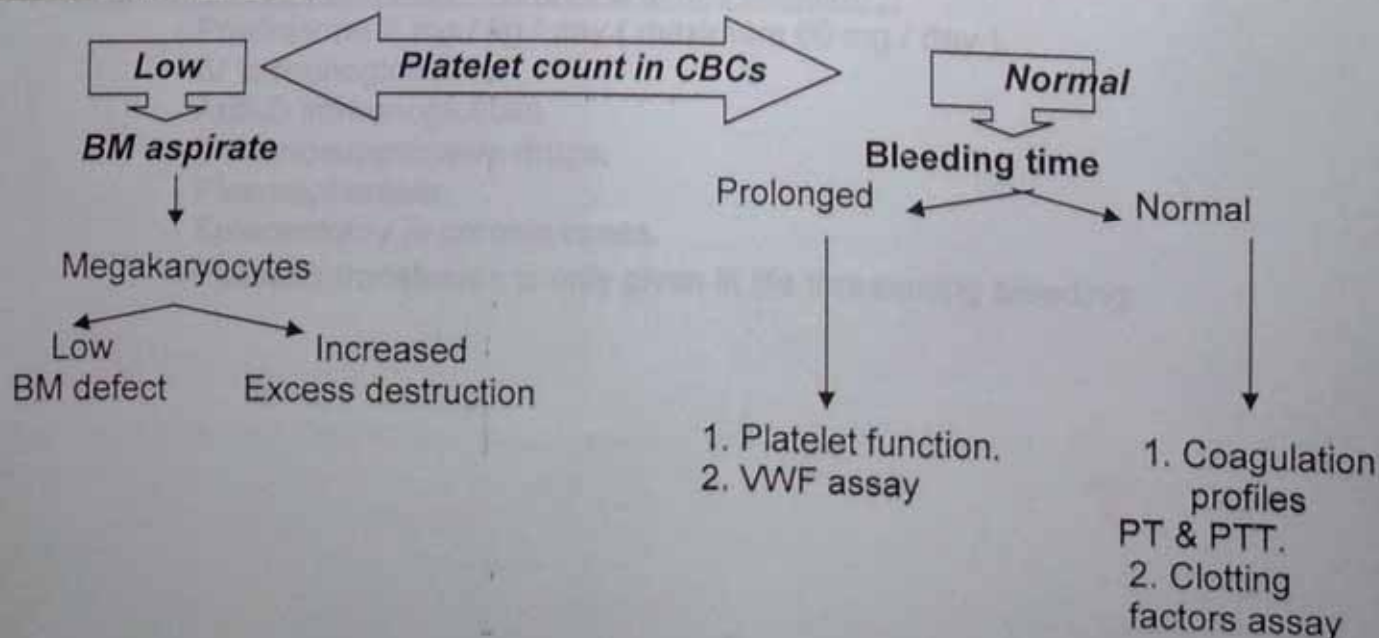
Congenital

1. Von-Willibrand disease.
2. Glanzmann's disease: due to deficiency of glyco-protein IIb & IIIa.
3. Bernard Soulier disease: due to deficiency of glyco-protein Ib (there are thrombocytopenia & thrombasthenia).

Acquired

1. Aspirin & Heparin in high concentration
2. Uremia.

Investigations



Immune thrombocytopenic purpura

Etiology

Auto-immune disease preceded by viral infections as measles, chicken pox, EB-virus or vaccination 1-3 weeks ago.

Clinical picture

1. History of exposure to viral infection 1-3 weeks ago.
2. Skin bleeding: petichae, purpura, ecchymosis or hematoma.
3. Mucus membrane hge.
4. Intra-cranial hge (ICH).
5. No organomegaly, lymphadenopathy or pallor at diagnosis.

Chronic ITP (persistent thrombocytopenia > 1 year)

May be idiopathic or a part of other diseases as SLE, HIV, Hodgkin's disease or Evan syndrome.

The onset is insidious with less severe hge than acute ITP.

The spleen is usually not palpable except with other diseases.

Investigations

1. Bleeding time (BT): ↑↑↑.
2. CBC: ↓↓↓ platelets.
3. Bone marrow aspirate (BM): ↑↑↑ megakaryocytes.

Treatment

I. Acute ITP:

- In mild cases (platelets > 40,000 & no active bleeding): no ttt is given but just follow up.
- In sever cases (platelets < 40,000 & active bleeding):
 - Prednisone 2 mg / kg / day (maximum 60 mg / day).
 - IV immunoglobulins.
 - Anti-D immunoglobulin
 - Immunosuppressive drugs.
 - Plasmapheresis.
 - Splenectomy in chronic cases.
 - Platelets transfusion is only given in life threatening bleeding.

Henoch Schonlein Purpura (Anaphylactoid Purpura)

Etiology

Allergic vasculitis of the small blood vessels in the skin, kidney, joints & GIT.

Clinical picture

1. **Age of onset**: 2-8 years.
2. **Sex**: male : female = 2 : 1.
3. **History of drug intake or upper respiratory tract infection**.
4. **Skin**: palpable purpuric eruptions mostly in the buttocks, extensor surfaces of the legs & forearms.
5. **Kidney**: nephritis → hematuria, oliguria, proteinuria & hypertension.
6. **Joints**: arthritis → red, hot, tender, swollen joints with complete loss of function.
7. **GIT**: Melena & colicky abdominal pain.

Investigations

1. **Bleeding time (BT)**: ↑↑↑.
2. **CBC**: normal platelet's count.
3. **Normal platelet's function**.

Treatment

No specific therapy.

1. **Prednisone**: gives symptomatic relief in severe cases & prevent hgc manifestations.
2. **TTT of complications if present**: as intussusceptions & nephritis.



The typical Henoch-Schönlein purpura rash with palpable purpura on an older child's lower extremities



Periorbital edema as commonly seen in young children with Henoch-Schönlein purpura

Pediatrics

Hematology

Hemophilia

Types

1. Hemophilia A (XL-R): due to $\downarrow\downarrow\downarrow$ factor VIIIc.
2. Hemophilia B (Christmas, XL-R): due to $\downarrow\downarrow\downarrow$ factor IX.
3. Hemophilia C (AR): due to $\downarrow\downarrow\downarrow$ factor XI

Hemophilia A

Etiology

- It is XL-R disease ($\downarrow\downarrow\downarrow$ factor VIIIc).
- 33 % have no family history with spontaneous mutations.

Degrees of severity

1. Mild: the level of factor VIIIc is 6-30 % of normal.
2. Moderate: the level of factor VIIIc is 1-5 % of normal.
3. Severe: the level of factor VIIIc is < 1 % of normal.

Clinical picture

1. Neonatal bleeding: bleeding from the umbilicus, after circumcision, after IM injection.
2. Hematoma: usually occurs on minimal trauma.
3. Hemarthrosis.
4. Hematuria.
5. Hemophilic pseudo-tumors: may occur in long bones, pelvis, fingers & toes due to sub-periosteal hges.



Complications

1. Serious life threatening hemorrhage as intracranial hge.
2. Formation of factor VIII inhibitors.
3. Complications of frequent blood transfusions.
4. Joint deformities.
5. Hemophilic pseudo-tumors.

Investigations

1. Bleeding time (BT): normal.
2. Prothrombin time (PT): normal.
3. Partial thromboplastine time (PTT): $\uparrow\uparrow\uparrow$.
4. Factor VIIIc assay.

Treatment

1. Avoid trauma.
2. Replacement therapy:

Product	Factor content	Approximate concentration of FVIII (u/ml)
GFFP	All factors	1
Cryoprecipitate	VIII & fibrinogen	5-10
FVIII concentrates	VIII	20-25

Another preparation to raise factor VIII is Desmopressin DDAVP that stimulates FVIII & vWF release from stores. Dose: 0.3-0.4 ug / kg IVI or intranasal.

3. Antifibrinolytic agent as ϵ -aminocaproic acid & Tranexamic acid to preserve clot.
4. Analgesics as acetaminophen (not aspirin) to control pain.

Von Willibrand disease

- Autosomal dominant disease.
- There is reduced vWF which promotes platelet adhesion & act as a carrier molecule for FVIIIc, protecting it from premature destruction $\Rightarrow$ abnormal platelet adhesion & lower factor VIII activity.

Investigations

1. **Bleeding time (BT):** $\uparrow\uparrow\uparrow$.
2. **CBC:** normal.
3. **Platelet functions:** There is defective platelet aggregation by restocetin corrected by vWF while aggregation by ADP & collagen is normal.
4. **Prothrombin time (PT):** normal.
5. **Partial thromboplastine time (PTT):** $\uparrow\uparrow\uparrow$.
6. **Low factor VIIIc & vWF activity.**

Treatment

As hemophilia A.

Glanzmann's disease

- o It is due to deficiency of **glycoprotein IIb & IIIa** $\rightarrow$ There is defective platelet aggregation by ADP & collagen while aggregation by restocetin is normal.

Bernard Soulier syndrome

- o It is due to deficiency of glycoprotein Ib receptors.
- o There is defective platelet aggregation by restocetin not corrected by vWF while aggregation by ADP & collagen is normal.
- o CBC : Thrombocytopenia & giant platelets.....why?

Vitamin K deficiency

Etiology

1. Inadequate intake.
2. Decreased gut flora : in preterm & prolonged use of broad spectrum antibiotics.
3. Obstructive jaundice $\rightarrow$ $\downarrow\downarrow\downarrow$ absorption.

Liver diseases

All coagulation factors are reduced

Disseminated Intravascular Coagulopathy (DIC)

Definition

- It is wide spread pathological intravascular clotting.

Etiology

1. Endothelial damage: due to hypoxia, acidosis, toxins, burns & irradiation.
2. Hemoconcentration.
3. Slow circulation.

Clinical picture

1. Very bad general condition.
2. Bleeding tendency.....why?.
3. Multi-organ failure.
4. Severe anemia.....why?.

Investigations

1. Bleeding time (BT): ↑↑↑
2. Prothrombin time (PT): ↑↑↑
3. Partial thromboplastin time (PTT): ↑↑↑.
4. CBC: severe anemia & thrombocytopenia.
5. Fibrin degradation products (FDPs): ↑↑↑

Treatment

1. TTT of the causative factors e.g. hypoxia, acidosis, shock, infection & dehydration.
2. Infusion of platelets, FFP, fresh blood.
3. Exchange transfusion especially in the newborn.
4. Fibrinogen IV → in cases of marked hypofibrinogenemia.
5. Heparin 100 U / kg / 4-6 hrs IV → when there is increased thrombosis as in purpura fulminans or hemolytic uremic syndrome.

Purpura fulminans: It is form of DIC in which the clotting phase predominate the picture → Vaso-occlusion → Gangrene of the extremities, nose, lips & ears.

Pancytopenia

Definition

- **Bicytopenia**: decrease in 2 of 3 components.
- **Pancytopenia**: decrease in 3 components

Etiology

1. Aplastic anemia.
2. Megaloblastic anemia either due to B12 or folic acid deficiency.
3. SLE.
4. Paroxysmal nocturnal hemoglobinuria (PNH).
5. Severe infection.
6. Brucellosis.
7. Sarcoidosis.
8. Fanconi anemia.
9. 2ry to bone marrow infiltration:
 - Metastatic cancer.
 - Myelofibrosis.
 - Osteopetrosis.
10. Splenic disorders (Hypersplenism):
 - Lymphoma.
 - Gaucher disease.
 - Nieman-Pick disease.
 - Congestion of the spleen.
 - Kala-Azar.

Clinical picture

1. Manifestations of anemia.
2. Bleeding tendency due to thrombocytopenia.
3. Repeated infection due to leukocytopenia.
4. $\pm$ Splenomegaly.
5. $\pm$ Lymphadenopathy.

Investigations

CBC:

- Pancytopenia.
- Macrocytic anemia....in megaloblastic.
- Reticulocytopenia.....(retics $< 1\%$).
- Reticulocytosis in hypersplenism.
- Thrombocytopenia.
- Neutropenia.

Absolute neutrophil count $< 500 / \text{mm}^3$.

ANC $< 200 / \text{mm}^3$ in very severe disease.

Bone marrow aspirate or biopsy to detect the underlying etiology.

Disorders of leukocytes

Component of the immune system

- B-lymphocytes: responsible for antibodies production.
- T-lymphocytes: responsible for cell mediated immunity.
- Phagocytic system: consists of circulating neutrophils, monocytes & tissue macrophages.
- Complement system acting synergistically with the immune system

Functions of the immune system

1. Prevent & retard local & systemic dissemination of microbial agents.
2. Prevent the development of autoimmune diseases & malignancy.

WBC count

- At birth: 38,000 / ul followed by rapid fall until the end of the 1st week.
- At 1 year: 6,000-17,500 / ul.
- In adult: 4,000-11,000 / ul.

Causes of leukocytosis

1. Physiologic

- a. Newborn.
- b. Exercise.

2. Acute infections.

3. Acute hemorrhage.

4. Malignancy: leukemia.

5. Hemolytic anemia & after splenectomy.

6. Connective tissue diseases: rheumatic fever & rheumatoid arthritis.

7. Metabolic: DKA & thyrotoxic crises.

8. Drugs: steroid, epinephrine & lithium.

N.B. the increase in WBC count may reach very high level $> 50,000 / \text{ul}$ this is called leukemoid reaction that has to be differentiated from acute leukemia.

	Leukemoid reaction	Acute leukemia
C/P	Infection	HSM & lymphadenopathy.
Anemia	-ve	+ve
Thrombocytopenia	-ve	+ve
BM aspirate	Normal or hyper cellular	Blast cells

Pediatrics

Hematology

Leucopenia

- Leucopenia is considered when WBC count is $< 4,000 / \text{ul}$.
- It may affect one or more lineages & it is possible to be severely lymphopenic or neutropenic without a reduction in the total WBC count

Neutropenia

- It is considered when PNL count is $< 1,000 / \text{ul}$ in infants between 2 weeks & 1 year, & less than $1,500 / \text{ul}$ beyond that age.

Mechanism

1. BM & stem cell maturation defect.
2. Suppression of neutrophil production:
 - a. Severe infection.
 - b. Malignant deposit in the BM.
 - c. Drugs: sulfonamides & anti-convulsions.
3. Increased destruction of neutrophils: Immune mediated: neonatal immune neutropenia & SLE.

Clinical picture

Severe neutropenia ($< 500 / \text{ul}$) has common clinical manifestations

1. High fever & toxemia.
2. Extensive oral ulcers.
3. Gram -ve septicemia.

Laboratory findings

1. CBC: neutropenia.
2. BM: marked reduction of myeloid series or maturation arrest.
3. Measurement of neutrophil antibodies.
4. Serologic tests for SLE.
5. BM culture for stem cells.

Treatment

1. Proper antibiotic therapy for eradication of infections.
2. Proper ttt of the underlying cause.

Esinophils

- They are produced & mature inside the BM $\Rightarrow$ migrate to tissue sites (epithelium of intestine specially the colon).
- The ratio of blood to tissue esinophils is about 1 : 100.
- In response to allergen or tissue parasites $\Rightarrow$ migrate to tissues (lung in BA, or intestinal wall following parasitic infestation).

Causes of esinophilia ($> 400 / \text{ul}$)

1. Allergy: BA, hay fever & eczema.
2. Parasitic infestations
3. Others: Hodgkin's, polyarteritis nodosa, Addison disease.

Causes of esinopenia

1. Cushing disease.
2. Steroid therapy.

Lymphocytes

Causes of lymphocytosis

1. **Physiologic**: between 4 months & 4 years

2. **Infections**:

Acute:

- a. Moderate in measles, rubella, mumps, typhoid fever.
- b. Marked in IMN, CMV, Toxoplasmosis & pertussis.

Chronic: TB.

3. **Acute lymphoblastic leukemia**.

Causes of lymphopenia

1. **Congenital B-cell deficiency** $\Rightarrow$ deficiency of immunoglobulins $\Rightarrow$ recurrent bacterial infections

2. **Congenital T-cell defect**: it is more severe than B-cell defect $\Rightarrow$ impaired cell mediated immunity $\Rightarrow$ repeated viral infections, TB, GVHD.

Leukemia

It is the most common form of childhood cancer.

Acute leukemia constitute 97 % of all childhood leukemia & consist of two types:

- Acute lymphoblastic leukemia (ALL) : 80 %.
- Acute non-lymphoblastic leukemia (ANLL) : 20 %.

Chronic leukemia constitute 3 % of childhood leukemia & consists of 2 types:

- Adult type of chronic myeloid leukemia (Philadelphia chromosome +ve).
- Juvenile type of chronic myeloid leukemia (Philadelphia chromosome -ve).

Incidence

1. 1 : 25,000 population.
2. Peak incidence: 2-5 years.
3. Account for 25-30 % of all childhood cancers.

Etiology

Unknown, but the following factors have been condemned:

1. **Ionizing radiations**.
2. **Chemicals** (benzene in ANLL).
3. **Drugs** (alkylating agents).
4. **Genetic considerations** because there is increase incidence in:
 - Identical twins.
 - In siblings.
 - With chromosomal abnormalities.
 - In genetically determined diseases as ataxia telangiectasia & agammaglobulinemia.

Clinical picture

1. General systemic effects:

- Fever.
- Anorexia.
- Loss of weight.

2. Hematologic effects due to BM invasion:

- Anemia → pallor, easy fatigability, dyspnea & tachypnea.
- Neutropenia → fever, ulceration of buccal mucosa & repeated infections.
- Thrombocytopenia → petichae, purpura

3. Manifestations from lymphoid system invasion:

- Lymphadenopathy.
- Hepatosplenomegaly.

4. CNS invasion:

↑↑↑ Intracranial tension (severe headache in the early morning, vomiting, blurring of vision, bilateral VI cranial nerve palsy & papilledema).

- Parenchyma involvement : hemi paresis, cranial nerve palsies & convulsions.
- Hypothalamic manifestations.
- Cerebellar manifestations.
- Intracranial hges.

5. Genitourinary tract involvement:

- Testicular enlargement.
- Renal involvement: hematuria, hypertension & renal failure.

Hematology

6. Gastro-intestinal involvement:

- Bleeding.
- Abdominal mass.
- Peritonitis & septic shock.

7. Bone & joint involvement:

- Generalized bone aches.
- Multiple osteolytic bone lesions.

8. Skin involvement:

- Skin masses can be presented especially in neonatal or ANLL.

9. Cardiac involvement: leukemic infiltration of the heart is very rare.**10. Lung involvement:** by blast cells.**Investigations****1.CBC:**

- Hb % : moderate to marked reduction.
- WBCs : low, normal or increased.
- Platelet's count: ↓↓↓.
- Blood film: Blast cells.

2.Bone marrow aspirate: diagnostic .**3.CXR:** - Mediastinal mass (T-cell leukemia).
- Lung infiltrates.**4.Skeletal survey:** transverse metaphyseal lines.**5.Blood chemistry:**

- Serum electrolytes.
- Renal functions.
- Serum uric acid.
- Liver functions.

6.CSF examination.**7.Coagulation profile:** decreased coagulation factors in ANLL.**8.Cardiac function:** ECG & echo-cardiography.**Risk factors in leukemia:**

Depends on several factors including:

- o Age: < 1 years & > 10 years.
- o Sex: males.
- o Organomegaly: huge spleen.
- o CXR: Mediastinal shadow (T-cell leukemia).
- o CNS involvement.
- o Testicular involvement.
- o Blast cells at diagnosis > 20,000 / mm³.
- o Platelet's count at diagnosis < 100,000 /mm³.
- o Hb % at diagnosis > 10 gm %.
- o Morphologic, cytogenetic & molecular characteristics

Treatment

General care

**** Supportive psychological care.**

**** Supportive medical care:**

- Packed RBCs.
- Platelets transfusion.
- Good hydration.
- Alkalinization of urine.
- Allopurinol 10 mg / kg / day.
- Broad spectrum antibiotics for eradication of infections.
- Live attenuated vaccines is contraindicated.
- Growth factors to correct neutropenia.

Specific therapy

- To induce clinical & hematological remission.
- To maintain remission.
- Prevention of CNS infiltration.
- Ttt of complications.

Therapy includes:

- Systemic chemotherapy.
- Intra-thecal chemotherapy as CNS prophylaxis.
- Radiotherapy.
- BM transplantation.

Assessment of remission :

- No symptoms or signs related to leukemia.
- Normal CBC.
- BM aspirate: < 5 % blasts.

Causes of death

- Organ failure.
- CNS infiltration & hges.
- Secondary malignancies.

Lymphomas

The 3rd most common tumor of childhood, after leukemia & brain tumors.

Types

1. Hodgkin's.
2. Non-Hodgkin's.

Hodgkin's Lymphoma

- **Age:** Rare < 5 years.
Peak incidence is at 13-35 years.

- **Sex:** Male : Female ratio = 2 : 1.

Clinical staging

Stage I :

Only one group of LNs....Or..... One extra-lymphatic site.

Stage II :

More than one group of LNs ± localized extra-lymphatic site
All should be at the same side of the diaphragm.

Stage III :

As stage II, but on both sides of the diaphragm ± spleen.

Stage IV :

Diffuse or disseminated involvement of one
or more extra-lymphatic organs ± associated LN enlargement.

Each stage is further divided into A or B.

A → no systemic symptoms.

B → Systemic symptoms as fever, night sweats & weight loss.

Clinical picture

1. **Painless swelling** of one or more superficial LN (firm, rubbery, not tender, discrete, single or multiple, with no regional inflammation).
2. **Mediastinal** \$ if mediastinal LNs are affected:
 - Persistent non-productive cough.
 - Congested non pulsating neck veins.
 - Hoarsness of voice.
 - Dysphagia in sever conditions.
3. **Constitutional symptoms** : Loss of weight, intermittent fever, anorexia & easy fatigability.
4. **Manifestations of extra-nodal involvement.**

Investigations

1. **LN biopsy** is diagnostic by identification of Reed-Sternberg cells in tumor tissues.

According to histo-pathology it is classified into 4 types :

- **Lymphocyte predominant type** (10-20 %) : Best prognosis.
- **Nodular sclerosing type** (50 %) : Favorable prognosis.
- **Mixed cellularity type** (40 %) : Less favorable prognosis.
- **Lymphocyte depletion type** (< 10 %) : Very bad prognosis.

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2. Other investigations as CXR, pelvi-abdominal U/S, CSF & BM aspirate are needed for staging of the tumor.

Treatment1. Conservative ttt:

- Packed RBCs for correction of anemia.
- Platelet concentrate for correction of thrombocytopenia.
- Broad spectrum antibiotics for eradication of infections.

2. Chemotherapy:3. Radiotherapy.**Non-Hodgkin's Lymphoma**

- It is more common than Hodgkin's lymphoma in young children. It is predisposed by immunodeficiency (congenital or acquired).
- EBV is the cause of African type of Burkett's lymphoma

Staging

Stage I: Single mass or LN (not in the mediastinum or the abdomen).

Stage II: Two masses on the same side of the diaphragm.

Or small 1ry GIT tumor ± mesenteric LN only.

Stage III: Two single tumors on both sides of the diaphragm.

Or any 1ry intra-thoracic.

Or extensive intra-abdominal disease.

Stage IV: CNS or BM infiltration.

Clinical picture

1. Painless unexplained swelling of cervical or supra-clavicular LN.

2. Rapidly growing tumor.

3. Other clinical manifestations are variable depends on the site of the 1ry tumor & extent of local & distant spread.

Investigations

As Hodgkin's lymphoma but pathologically it is classified into small & large cell types.

Treatment

As Hodgkin's lymphoma but with different protocol of chemotherapy.
CNS prophylaxis is essential for T-cell & Burkett's type

Burkett's LymphomaAfrican type:

- Affects children previously infected with EBV.
- It involves bones of the face as maxilla & orbit.
- It is very sensitive to irradiation & chemotherapy, but has high tendency to relapse.

American type:

- Affects young adults.
- Not associated with EBV.
- Usually of abdominal origin.
- Higher BM & CNS involvement.

Lymphadenopathy

Etiology

A. Non-specific reactive hyperplasia.

1. Infections:

• Viral:

- Infectious mononucleosis.
- Cytomegalovirus.
- Rubella & rubeola.
- Varicella.
- Herpes simplex.

• Bacterial:

- TB.
- Brucella.
- Salmonella.
- Staph & streptococcus.

• Protozoa: e.g. toxoplasmosis.

• Spirochete: e.g. syphilis.

• Fungal: e.g. coccidiomycosis.

2. Connective tissue disorders:

- o Rheumatoid arthritis.
- o SLE.
- o Kawasaki disease

3. Hypersensitivity states:

- o Serum sickness.
- o Drug reaction e.g. INH, antithyroid.



B. Lymphoproliferative disorders

1. Neoplastic disorders:

- o Hodgkin & non- Hodgkin's lymphoma.
- o Leukemia.
- o Metastases.
- o Histiocytosis.

2. Storage diseases:

- o Nieman-Pick disease.
- o Cystinosis.

3. Granulomatous diseases:

- o Sarcoidosis.
- o Chronic granulomatous disease.

4. Miscellaneous:

- o Hyperthyroidism
- o Post-vaccination

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Management

History

- Duration of lymphadenopathy.
- History of infection.
- History of systemic complaint e.g. Wt loss, night sweating, arthritis or arthralgia, generalized bone aches

Examination

- **General examination** for evidence of hematological disease e.g. pallor, purpura & hepatosplenomegaly.
- **Lymph node examination:**
 1. **Site:**
 - Enlarged tonsillar or inguinal LNs is most likely due to localized infection.
 - Enlarged supraclavicular & axillary's LNs are most likely to be of a serious nature.
 2. **Size:**
 - LN > 2.5 cm & that increase in size should be considered pathologic.
 3. **Number:**
 - Is it localized or generalized.
 - Or start localized then become generalized.
 4. **Consistency:**
 - Malignant LNs are usually firm or rubbery.
 - Fluctuant & warm LNs usually associated with infections.
 5. **Tender or not**
 - Tender LNs usually associated with infections
 - Malignant LNs are usually not tender.
 6. **Relation to each others:**
 - tuberculous LNs usually matted together.
 7. **Relation to underlying structures:**
 - If LNs are attached to underlying structures usually malignant
 8. **Relation to overlying skin:**
 - Tuberculous LNs may be attached to overlying skin & may be associated with ulcer.

Investigations

- **CBC & ESR.**
- **Skin test:** for TB & Fungal infection.
- **Bacteriological culture:** for regional lesion.
- **Serologic test** for Toxoplasmosis, CMV & EBV.
- **Radiological investigations:** CXR, Abdominal sonar & CT if indicated.
- **Bone marrow aspiration or biopsy** may be needed if hematological disease is suspected.
- **LN biopsy if:**
 - a. Malignancy is suspected.
 - b. Laboratory investigations is not conclusive.
 - c. Size > 2.5 cm.
 - d. Persistent LN or has progressive course.
 - e. Not responding to antibiotics for 1 month.

Splenomegaly

- The tip of the spleen is frequently palpable in normal infants & young children up to 3-4 years of age. At older age, a palpable spleen usually indicates splenic enlargement.
- Palpable spleen may be due to visceroptosis rather than splenomegaly.

Etiology

A. Infections.

Acute

- Viral:
 - Infectious mononucleosis (IMN).
 - Cytomegalovirus (CMV).
- Bacterial:
 - Subacute bacterial endocarditis (SBE).
 - Salmonella (typhoid fever).
- Protozoa: e.g. malaria
- Rickettsial.

Chronic:

- Bacterial:
 - Subacute bacterial endocarditis (SBE).
 - TB.
 - Brucellosis.
- Spirochete: e.g. syphilis
- Protozoal: e.g. malaria, toxoplasmosis & Schistosomiasis.
- Fungal: e.g. coccidiomycosis

B. Hematological disorders

1. Hemolytic anemia:

- Thalassemia.
- Spherocytosis.
- Splenic sequestration in sickle cell ane

2. Extramedullary hematopoiesis as:

- Myelofibrosis.
- Osteopetrosis.

3. Myeloproliferative disorders: e.g. polycyther

C. Infiltrative disorders

1. Non-malignant:

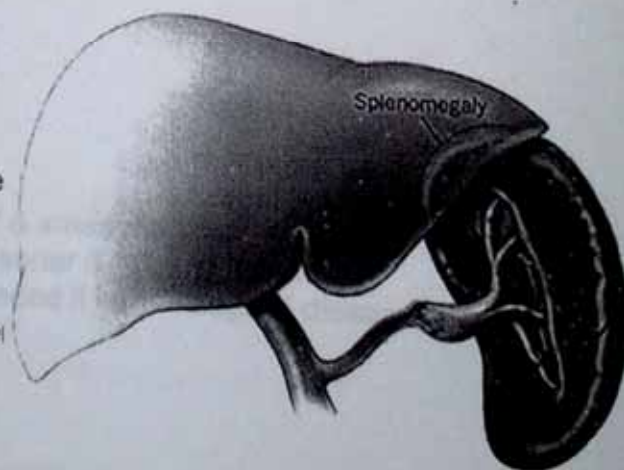
- Histiocytosis.
- Storage disease:
 - Gaucher's disease.
 - Niemann-Pick.
 - Mucopolysaccharoidosis.

2. Malignant as:

- Leukemia.
- Lymphoma.

D. Congestive splenomegaly

- All causes of portal hypertension.....see notebook of GIT.



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E. Hypersensitivity states

- Serum sickness.
- Connective tissue disorders:
 - Rheumatoid arthritis.
 - SLE.

F. Primary splenic disorders

- Cysts.
- Benign tumors (hemangioma).
- Hemorrhage in the spleen (e.g. subcapsular hematoma).

Management**History**

- Fever & rigors → infection.
- History of neonatal umbilical sepsis → portal vein thrombosis.
- History of jaundice → liver disease.
- Generalized bone aches & bleeding tendency → leukemia.
- +Ve family history of CHA.
- History of trauma → subcapsular hematoma of the spleen.

Examination

- Size of spleen, consistency, tenderness.
- Hepatomegaly.
- Lymphadenopathy.
- Fever.
- Purpura.
- Jaundice.
- Manifestations of rheumatoid arthritis & SLE.
- Splinter hge.
- Cardiac murmur.

Investigations

- CBC & ESR.
- Skin test: for TB & Fungal infection.
- Bacteriological culture: for regional lesion.
- Serologic test for Toxoplasmosis, CMV, EBV & smear for malaria.
- Radiological investigations: CXR, Abdominal sonar & CT if indicated.
- Bone marrow aspiration or biopsy may be needed if hematological disease is suspected.
- Liver function tests.
- Investigations of portal hypertension.
- Enzymatic assay for Gaucher.
- C3, C4 & ANA If connective tissue diseases is suspected.
- LN biopsy if significant lymphadenopathy:
- Biopsy: Partial biopsy & splenic aspiration are rarely performed because there is a significant risk of bleeding.

DIFFERENTIAL DIAGNOSIS OF ABDOMINAL MASSES IN INFANTS AND CHILDREN

I- GENITOURINARY DISORDERS

A. Renal disease

- Mass in the loin except in kidney malformations. Associated findings may be abdominal pain and tenderness, hematuria, hypertension, evidence of urinary tract infections, deterioration of renal functions
- Causes
 1. Hydronephrosis
 2. Polycystic kidney.
 3. Solitary renal cysts
 4. Renal vein thrombosis
 5. Ectopic or horse-shoe kidney
 6. Perinephric abscess

B- Bladder distension

- Mass is globular, in middle line, usually below umbilicus
- Causes
 1. Posterior urethral valve (more in neonates)
 2. Anticholinergic drugs
 3. Spinal cord lesions: tumors, trauma, congenital abnormalities
 4. Infection of bladder, urethra, or pelvis

C-Urachal Cyst

Palpated as middle line cystic swelling below the umbilicus, attached to the abdominal wall

D-Uterine enlargement

Hydrometrocolpos (prepubertal) and Hematocolpos (post-pubertal): Due to imperforate hymen, distension of the uterus by accumulated secretions and menses. Palpated as pelviabdominal mass

E-Ovarian disorders

Ovarian cysts and tumors are uncommon in childhood

II- NEOPLASMS

A-Wilms' tumor

*Wilm's tumor is a mixed neoplasm composed of metanephric blastema with stromal and epithelial derivatives at various stages of differentiation.

*The most common features at presentation are:

- Abdominal mass - in 80% of patients, the mass is lateral and nodular and may be visible on inspection
- Abdominal pain in 30% of patients - usually vague and poorly defined
- Haematuria in 25% of patients, usually microscopic

*Metastases are present in 20%. They mostly affect the liver and lungs, and occasionally, bone.

*General symptoms are commonly anorexia, weight loss, fever and anaemia.

*There may be hypertension or erythrocytosis.

B-Neuroblastoma

*A tumor derived from neural crest tissue the most common sites are:

- 50% adrenal medulla
- 25% abdominal sympathetic ganglia

*Clinical features:

Depend upon the site of the primary tumor and the extent of metastases; the symptoms can be very varied. Half of cases present with advanced disease. Local infiltration, lymphatic spread, and haematogenous spread, particularly to liver, lungs and bone, is common.

*General effects of malignancy: pallor - anemia - fever, weight loss, anorexia, irritability, and failure to thrive

*Local tumor effects:

- An abdominal mass is common - it may cross the midline and be difficult to distinguish from the liver
- Local invasion may cause the cauda equina syndrome, or paraplegia

*Metastatic spread: proptosis, Horner's syndrome, dysphagia, lung collapse, bone pain and pathological fracture, periorbital bruising looking like a black eye is seen in children, skin nodules

*Increased catecholamines secretion: flushing, cerebellar ataxia, diarrhoea, hypertension is rare

C-Lymphoma

Enlargement of the liver and spleen are common, but abdominal lymph nodes are frequently enlarged

D-Teratoma

Abdominal mass high in the retroperitoneal region, usually in first two years of life. X-ray show spotty calcification

E-Mesoblastic nephroma

Rare embryonic tumor, usually presents at birth

F-Rhabdomyosarcoma

Rare, highly malignant tumor that originates from striated muscle.

III- **INTESTINAL DISORDERS**

A-Fecal material

In constipation, masses of impacted stools are palpable in the left lower quadrant mobile, disappear after enema

B-Intussusception

Other symptoms such as pain and vomiting are prominent than the mass that is felt in right lower or upper quadrant

C-Intestinal duplication

In addition to the mass, abdominal pain, vomiting, and GIT hemorrhage may be present

D-Malrotation with volvulus

The sudden onset of pain and vomiting herald this serious event

E-Bezoar

In premature infants fed milk with high casein content may develop lactozoars. Hair ingestion may also result in gastric masses

F-Intestinal tumors

Lymphomas, leiomyosarcomas and other tumours are uncommon

G-Inflammatory lesions:

1. Tabes mesenterica
2. Appendicular mass : inflamed appendix with an adherent covering of omentum and small bowel. The history is similar to that of appendicitis with a longer duration since onset. Examination reveals a mass in the right iliac fossa.
3. Abscess

H-Pyloric stenosis

Occurs in neonates and first months of life ; characteristic "projectile" vomiting .Examination reveals the distended stomach and a smooth ovoid mass just below the right costal margin, which is the hypertrophied pylorus.

IV -BILIARY DISORDERS

A-Choledochal cyst

Mass in right upper quadrant with jaundice and pain

B-Hydrops of gall bladder

Infants with acute hydrops present with poorly localized continuous abdominal pain and mass in right upper quadrant

C-Distended gall bladder

Occasionally occurs in cystic fibrosis

V-MISCELLANEOUS CAUSES

A-Pancreatic cyst

Following blunt trauma to the abdomen, mass in epigastrium or upper left quadrant with or without ascites

B-Abscesses

Abdominal abscesses are frequently associated with fever, abdominal discomfort or pain, anorexia, +/- vomiting and diarrhea

C-Adrenal hemorrhage

More in neonates, felt as loin mass

D-Aortic aneurysm

Rare, mass is pulsatile

BLOOD AND BLOOD COMPONENT TRANSFUSION

Differentiation should depend on

- History and physical examination
- Investigations should include CBC, ESR, liver and renal functions, abdominal sonar, CT abdomen and MRI if needed
- Other specific investigations may include IVP, isotopic scan
- Assessment of urinary catecholamines if suspect neuroblastoma

THE AGE OF THE AFFECTED CHILD IS IMPORTANT:

Neonates	Early childhood	Adolescents
- Hydronephrosis an/or enlarged bladder (PKD, PUV, UPJ obstruction)	- Tumours ~Wilms',	- Fecal material
- Renal vein thrombosis	- neuroblastoma,	- IBD
- Hepatoma/hemangioma	- rhabdomyosarcoma, non-	- Abscess
- Storage disease	- Hodgkin's lymphoma,	- Tumours
- Choledochal cyst	- hepatic, ovarian)	- Ovarian cyst/torsion
- Duplication	- Pyloric stenosis (3-6 wk)	- Pancreatic
- Ovarian cyst	- Intussusception (3-6 mo)	- pseudocyst
- Teratomas	- Duplication cysts	- Choledochal cyst
- Hydrocolpos/hematocolpos	- Mesenteric cysts	- Bladder distension
- Adrenal hemorrhage	- Hydronephrosis	- Hydrometrocolpos
- Mesenteric/omental cyst	- Renal malformation	
Mesoblastic nephroma	- Fecal material	
- Volvulus	- Choledochal cyst	
- Other congenital lesions	- Bladder distension	
	- Pancreatic pseudocyst	
	- Other congenital lesions	

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BLOOD AND BLOOD COMPONENT TRANSFUSION

Facts about blood:

- Blood is composed of plasma, water and cellular components (red blood cell, white blood cells and platelets)
- Blood and blood products are used to treat accident and burn victims, cancer patients and other patients undergoing surgeries and medical treatments.
- Red blood cells can be stored for up to 42 days
- Platelets can be stored for only five days
- Frozen plasma can be stored for as long as one year
- Persons belonging to the O -ve blood group are called universal blood donors.
The RBCs of a universal blood donor may be transfused to anyone regardless of their blood type.
- The plasma of those belonging to the AB blood group may be transfused to anyone regardless to their blood type.
- More than 90% of transfusion complications have been attributed to the presence of leucocytes in allogeneic blood.
- The maximum allowable time for the transfusion is four hours.
- The transfusion rate should be determined by the patient clinical status.
- Because blood donations often are separated into several components (RBCs, plasma, platelets, for instance).
- One donation can help save three lives.

Red Blood cell transfusion

They are the most frequently transfused blood component.

Indications:

- 1- Acute hemorrhage: blood loss > 25% of the circulating blood volume.
- 2- Symptomatic anemia (hemoglobin < 7-8 gm / dl) and patients with chronic anemia secondary to bone marrow suppression.
 - The decision to transfuse RBC should be based only on blood hemoglobin levels because children with chronic anemia may be asymptomatic despite low hemoglobin level
 - Factors considered in the decision to transfuse RBCs other than Hb level are: 1) Patient's symptoms and signs, 2) Cause of anemia, 3) Alternative therapies e.g. recombinant human erythropoietin (EPO) therapy which has reduced the need for RBC transfusion in certain diseases e.g. chronic renal insufficiency.
 - RBCs transfusion for thalassemia and sickle cell anemia (see chapter ...). The dose recommended for pediatric population is 10-15 mL / Kg. The patients with active bleeding or hypersplenism might require additional RBC

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transfusion to maintain or increase their hemoglobin.

In chronic RBCs transfusion:

- Cross matching should be performed before each transfusion to decrease the alloimmunization and transfusion reaction.
- Packed RBCs should be relatively fresh
- Leukoreduction should be used (see below).
- Transfused blood should be screened and the patient should be vaccinated.

Neutrophil (Granulocyte) transfusions

- Infected neutropenic patients usually respond to antibiotics alone provided bone marrow recovers early in infection.
- Newly diagnosed leukemia respond to induction chemotherapy, they do not need granulocyte transfusion. In contrast, infected children with sustained bone marrow failure and severely neutropenic ($< 0.5 \times 10^9$ L) may benefit when granulocyte transfusion are added to antibiotics.
- Children with qualitative neutrophil defects may need granulocyte transfusion added to the antibiotics when presenting with progressive life threatening infection.

These disorders are chronic and because of the risk of alloimmunization granulocyte transfusion are recommended only when infection are clearly unresponsive to antimicrobial drugs.

Platelet transfusions

- Platelets can be obtained from a unit of whole blood or collected by apheresis.
- The volume, platelet content and dose of platelets will depend on the method of collection used.
- The storage time is 5 days (once pooled the storage time becomes 4 hours).

Indications for platelet transfusion:

- Treatment of bleeding or its prevention prior to an invasive procedure in patients with platelet count $< 50 \times 10^9$ L.
- Bleeding prophylaxis in patients with platelet count $< 10 \times 10^9$ L secondary to bone marrow suppression.
- In patients with congenital or acquired platelet dysfunction, platelet transfusion are justified only if significant bleeding occurs. Because PLT dysfunction may be present long time and repeated transfusion may lead to alloimmunization and refractoriness. In these patients, alternative therapies, particularly desmopressin acetate should be considered to avoid PLT transfusions.
- In the absence of life threatening bleeding, platelet transfusion may be

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contraindicated in idiopathic thrombocytopenic purpura and thrombotic thrombocytopenic purpura.

Plasma transfusion

- Plasma is obtained from a unit of whole blood and contains approximately 200-220 ml/bag. *Plasma dose is 15 ml / Kg.*
- It is stored frozen for up to one year.
- Transfusion of fresh frozen plasma (FFP) is used in the treatment of bleeding or prior to an invasive procedure in patients with acquired or congenital coagulation factor deficiencies (II, V, VII, X).
- Factor XIII and fibrinogen deficiencies are treated with cryoprecipitate.
- Transfusion of FFP or cryoprecipitate is no longer recommended for treatment of patients with severe hemophilia A or B, because safer factor VIII and IX concentrates are available. Moreover, mild to moderate hemophilia A and certain types of von Willebrand's disease can be treated by DDAVP.
- The use of plasma is also indicated for fluid replacement during plasma exchange in patients with thrombotic thrombocytopenic purpura.
- FFP is used for rapid reversal of warfarin effects in patients who are actively bleeding.
- FFP contains several anticoagulant proteins (antithrombin III, protein C and protein S) whose deficiencies have been associated with thrombosis. FFP may be used as a replacement therapy in these patients.

Cryoprecipitate

- Cryoprecipitate is prepared from a unit of FFP
- Cryoprecipitate contains only fibrinogen and factors VIII and XIII
- Transfusion of cryoprecipitate is indicated for treatment of bleeding or its prevention prior to an invasive procedure in patients with hypofibrinogenemia.
- Cryoprecipitate is also used in the preparation of fibrin glue which is a topical adhesive used for certain surgical procedures and consists of a mixture of thrombin and cryoprecipitate.

Risks of blood transfusion

I) Infectious risks:

transmission of:

- HIV
- Hepatitis B & C
- CMV (can be eliminated by transfusing cellular blood products filtered with leucocyte filters)
- Syphilis
- Parvovirus B19

- Epstein-Barr virus
- Chagas disease

II) Risks of non-infectious nature

- Febrile transfusion reaction
- Fluid overload
- Graft versus host disease
- Electrolytes and acid base imbalances
- Iron overload
- Increased susceptibility to oxidant damage
- Exposure to plasticizers
- Hemolytic transfusion reaction (immediate or delayed)
- Immunosuppression and alloimmunization.

N.B.

Patients known to have immune dysfunction are at increased risk of post transfusion graft versus host disease. For these patients all cellular blood components should be irradiated before transfusion, but frozen acellular products such as FFP do not require it.

Leukoreduction

What is leukoreduction?

It is a process of removing > 99.9% of WBCs from cellular blood components (red cells and platelets).

Method for leukoreduction:

Almost all red cells are leukoreduced using a specific filter. Washing was used as a method for leukoreduction but is not very efficient resulting in only 90% WBCs removal.

Indications:

- 1- Recurrent fever chill reactions.
- 2- Immediate or delay alloimmunization to HLA antigens
- 3- The risk of CMV transmission.

Acute abdominal pain

In infancy:

A. Medical causes:

1. Feeding errors:

- Underfeeding → Hunger pains.
- Overfeeding due to abdominal distension.
- Aerphagia.
- irritable mothers → they secrete catecholamine in their breast milk that pass to their infants → vomiting & abdominal pain.
- Milk allergy.

2. Urinary tract troubles:

- UTI.
- Renal stones.

3. Infections & Infestations:

- Entameba.
- Giardiasis.
- E-coli.

B. Surgical causes:

- Intussusception.
- Congenital intestinal anomalies as stenosis or malrotation.
- Visceral hernias.
- Meckel's diverticulum.

In childhood:

A. Medical causes:

1. local abdominal disease:

a. Liver:

- Viral hepatitis.
- Liver abscess.
- Congestive HF.

b. Kidney:

- UTI.
- Stones.

c. Spleen:

- Congestive splenomegaly.
- Sequestration & vaso-occlusive crises in sickle cell disease.

d. Intestine:

- Heavy parasitic infestations.
- Regional enteritis.

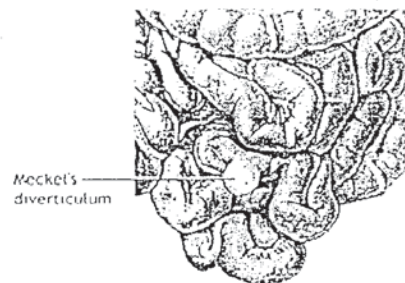
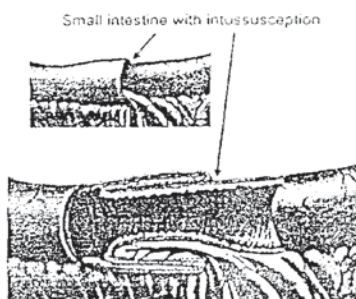
e. Lymph nodes: mesenteric adenitis & TB.

f. Pancreas: acute pancreatitis.

g. Gall bladder:

- Cholecystitis.
- Gall stones as in CHA.

h. Peritonitis.



2. General causes:

- a. DKA.
- b. Rheumatic fever.
- c. SBE.
- d. Lead poisoning.
- e. Porphyria.
- f. Hypoglycemia.

3. Referred pain from other diseases:

- a. Lower lobar pneumonia with basal pleurisy.
- b. From spine.
- c. From the pelvis: ovaries & testes.

B. Surgical causes:

1. Appendicitis.
2. Hernias (inguinal or umbilical).
3. Persistent intestinal anomalies from infancy.

Recurrent abdominal pain

A. Medical causes:1- Local abdominal disease:

1. Worm infestation: ascaris or Giardiasis
2. Chronic infection: E. coli or abdominal TB
3. Urinary tract infection or obstruction
4. Meckel's diverticulitis
5. Regional "enteritis
6. Peptic ulcer
7. Sickle cell anemia (splenic or mesenteric infarction)
8. Gluten enteropathy with celiac crisis
9. Helicobacter pylori infection which give rise to recurrent abdominal colic's and peptic ulcers.

2- General causes:

1. Familial Mediterranean fever
2. Diabetic ketoacidosis
3. Lead poisoning
4. Porphyria
5. Visceral epilepsy
6. CNS: tumors or encephalitis.

3- Psychiatric causes:

1. School problem
2. Home problem

- Children always present with repeated attacks of vomiting and abdominal pain in the morning (school problem) or on returning home (home problem) due to maltreatment or malbehaviour of the teachers and colleagues or due to stiff parental treatment of frustrated child.

B. Surgical causes:

1. Recurrent Intussusception
2. Recurrent hernia
3. Intra-abdominal tumor
4. Partial malrotation of the intestine.

Diagnosis

1. Careful history taking including family history.
2. Careful nutritional history as regard type of milk, amount, supplement feed, weaning, food additives ... etc
3. Thorough psychiatric history and evaluation to detect any school or home problem.
4. Meticulous and detailed history about type of pain, its character, radiation, relation to food, what increases and what relieves.
5. Through clinical examination of abdomen, GIT and other systems.
6. Complete urine and stool analysis.
7. Occult blood in stools.
8. Complete blood picture to detect viral and bacterial infections.
9. Blood film, hemoglobin electrophoresis to detect hemolytic anemia.
10. Tuberculin test.
11. Random blood glucose and glucose in urine with ketoses to detect diabetes.
12. X-ray for abdomen, chest, spine and urinary tract.
13. Abdominal and pelvic U/S.
14. Tests to detect typhoid fever and brucellosis.
15. Other specific tests for each disease mentioned before in the causes.

Treatment

- Is directed mainly towards the specific cause or infection according to the results of examination and investigations.

Constipation

Cause	Example
1. <u>Non-organic</u> (functional)	▪ Dietary (little water and /or fiber intake) ▪ Idiopathic
2. <u>Organic</u>	
1-Intestinal	▪ Hirschsprung disease ▪ Anal- rectal stenosis ▪ Stricture ▪ Volvulus ▪ Pseudo- obstruction
2- Drugs	▪ Narcotic ▪ Antidepressants ▪ Vincristine ▪ Antihistaminic
3- Metabolic	▪ Dehydration ▪ Cystic fibrosis (meconium ileus equivalent) ▪ Hypothyroidism ▪ Hypokalemia ▪ Hypercalcemia
4- Neuromuscular	▪ Myotonia dystrophy ▪ Spinal cord lesions (tumors, spina bifida) ▪ Amyotonia congenita ▪ Anorexia nervosa
5- Psychiatric	



Differential diagnosis of bleeding per rectum

Infant	Child	Adolescent
1. Dysentery 2. Bacterial enteritis 3. Milk protein allergy 4. Intussusception 5. Anal fissure	1. Dysentery. 2. Bacterial enteritis 3. Anal fissure 4. Intussusception 5. Henoch- schonlein purpura 6. colonic polyps	1. Dysentery 2. Bacterial enteritis 3. Inflammatory bowel disease 4. Colonic polyps

Differential diagnosis of hematemesis in pediatrics

Infant	Child	Adolescent
1. Reflux esophagitis 2. Stress ulcer 3. Gastritis (Helicobacter, other bacteria or drugs) 4. Bleeding disorders	1. Gastritis 2. Stress ulcer 3. Esophageal varices 4. Peptic ulcer 5. Reflux esophagitis 6. Foreign body 7. Bleeding disorders	1. Gastritis 2. Stress ulcer 3. Esophageal varices 4. Peptic ulcer

Causes of gastrointestinal obstruction

Site	Cause
Esophagus	1. <u>Congenital</u> a. esophageal atresia b. vascular rings 2. <u>Acquired</u> a. Esophageal stricture as after severe reflux. - b- Foreign body.
Stomach	1. <u>Congenital</u> a. Antral webs b. Pyloric stenosis 2. <u>Acquired</u> a. Bezoars / foreign body b. Pyloric stricture
Small intestine	1. <u>Congenital</u> 1. Duodenal atresia 2. Annular pancreas 3. Malrotation 4. Volvulus 5. Healed Atresia 6. Meconium ileus 7. Inguinal hernia 2. <u>Acquired</u> 1. Adhesions post surgery 2. Crohn's disease 3. Intussusception 4. Meconium ileus equivalent
Colon	1. <u>Congenital</u> 1. Meconium plug 2. Hirschsprung disease 3. Colonic atresia, stenosis 4. Imperforate anus 5. Rectal stenosis 6. Pseudo-obstruction 2. <u>Acquired</u> - Ulcerative colitis (toxic megacolon)

Vomiting

Definition

- It is forceful expulsion of gastric contents through the mouth.
- ❖ Regurgitation: is the effortless event.
- ❖ Rumination: is return of gastric contents to mouth + Rechewing and reswallowing. It occurs in psychotics and mentally retarded.

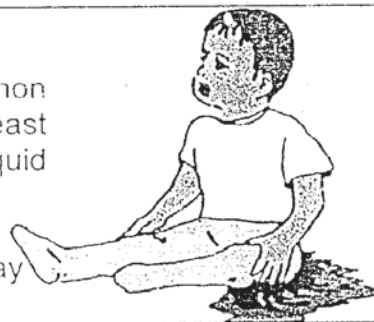
Age	Causes	Features
Infant (common)	❖ Overfeeding	○ Overweight + intake more than needs
	❖ Gastroenteritis	○ V+ Diarrhea of acute Onset
	❖ Gastro-esophageal Reflux	○ Non forced vomiting
	❖ Anatomic obstruction	○ Triad of intestinal obstruction = V + constipation + abdominal distension
	❖ Systemic infection	○ Fever + symptoms of relevant infection
Child (common)	❖ Gastroenteritis	○ V+ diarrhea of acute onset.
	❖ Systemic infection	○ Signs of the underlying Disease
	❖ Toxins or drugs	○ History
	❖ Hepatitis	○ Abdominal Pain + fever. Jaundice and dark urine may appear few days later.
	❖ Peptic ulcer	○ Epigastric pain related to meals ± hematemesis
	❖ ↑intracranial pressure	○ Projectile vomiting + Headache ± neurological signs of each cause
Adolescent (common)	❖ Cyclic vomiting	○ Is usually an exclusion diagnosis
	❖ Gastroenteritis	○ V+ Diarrhea of acute onset
	❖ Systemic infection	○ As above
	❖ Toxins or drugs	○ History
	❖ Inflammatory bowel disease	○ Diffuse crampy abdominal pain ± bloody mucoid diarrhea of long duration
	❖ Appendicitis	○ Acute onset abdominal pain starting all over the abdomen then localizing to Rt. iliac fossa + tender McBurney's point
	❖ Migraine	○ Hemi cranial headache + Autonomic manifestations

	❖ Bulimia	○ Excess CHO intake + induced vomiting
	❖ Hepatitis	○ Abdominal Pain + fever. Jaundice and dark urine may appear few days later.
	❖ Peptic ulcer	○ Epigastric pain related to meals ± hematemesis
	❖ Biliary colic	○ Rt. Hypochondria colicky pain ± obstructive jaundice
	❖ Renal colic	○ Loin pain ± urinary symptoms
	❖ Cyclic vomiting	○ As above

Diarrhea

Definition

- Frequent passage (> 3 motions / day) in non breast-fed or more than normal habit in breast fed infants) of large amount of liquid stool (liquid enough to take the shape of the container).
- ❖ **Mild diarrhea** : Purging rate of 50-70 ml / kg / day
- ❖ **Moderate diarrhea** : Purging rate of 70-90 ml / kg/day
- ❖ **Severe diarrhea** : Purging rate > 90 ml / kg/day



- Frequent small volume motions following feeding may be just a result of enhanced gastro-colic reflex.
- **Dysentery = Diarrhea + tenesmus + mucus ± blood**
- Up to 7 times/D of formed stools can be considered normal in infants

Etiology

❖ Infectious:

A. Enteral Infections "1ry GE".

1. Bacterial

- Salmonella
- Pathogenic E-coli
- Campylobacter
- Staphylococcus
- Cholera

2. Viral:

- Rota-virus (the most common).
- Entero-viruses "ECHO and Coxsackie"
- Adeno-virus

3. Fungal :

- Monilia Albicans

4. Parasitic :

- Entameba, Giardia lamblia
- Bilharzial

B. Toxic (complicated) GE

1. Diarrhea & vomiting are severe.
2. Fever $\Rightarrow$ due to toxemia & dehydration
3. Dehydration $\Rightarrow$ Why?
4. Acidosis or alkalosis.
5. Electrolyte imbalance
 - a. Hyponatremia.
 - b. Hypokalemia.
 - b. Hypocalcaemia.
 - d. Hypomagnesaemia.

Complications

1. Dehydration: The most serious complication.
2. Electrolyte imbalance (Hyponatremia, Hypernatremia & Hypokalemia are the most common).
3. Acid base disturbances (metabolic acidosis is common).
4. Malnutrition $\Rightarrow$ as a result of starvation & recurrent attacks
5. Intercurrent infections.
6. Lactose intolerance
7. D.I.C.
8. Pre-renal failure & acute tubular necrosis
9. Cerebral damage Due to
 - o Thrombosis
 - o DIC $\rightarrow$ I.C Hge
 - o Hypernatremia
10. Tetany

Due to Hypocalcaemia or Hypomagnesaemia or alkalosis during correction of acidosis
11. Iatrogenic

e.g. Fluid overload , electrolyte disturbance & acid-base disturbance
12. Immune mediated disorders
 - o Reactive arthritis.
 - o Guillian Barre \$.
 - o Immune hemolytic anemia.
 - o Glomerulonephritis.
13. Systemic effects:
 - o Septicemia
 - o Bacteremia.
 - o Endocarditis if the infant has CHD.
 - o Hemolytic Uremic \$.....see notebook of nephrology.
 - o Hepatitis (amebic or pyogenic).
 - o Meningitis or encephalitis (rare).

Investigations

1. Stool analysis & culture

For pus cells – RBCs , Giardia & amoeba

2. CBC

For Hct $\rightarrow$ hemoconcentration

3. Blood gases:

For acidosis or alkalosis.

4. Urine analysis & renal function

5. Serum electrolytes Na, K, Ca and Mg

Treatment

The main lines of treatment are :

- ❖ Prophylactic.
- ❖ ttt of the cause
- ❖ Correction of dehydration & acidosis
- ❖ Feeding
- ❖ Symptomatic

A. Prophylactic ttt:

- Encourage breast feeding.
- Delay weaning in hot weather.
- Avoid contamination.
- Vaccination against rotavirus.

B. ttt of the cause

- Trimethoprim-sulfamethoxazole combination 48 mg / kg / D orally in divided doses
- Ampicillin 50-100 mg/kg/D orally divided / 6 hrs
- Chloramphenicol
- Specific ttt for Entameba & Giardiasis : Metronidazole (flagyl)
- For campylobacter : Erythromycin.

C. Feeding in G.E.

1. Breast feeding
 - continue on breast feeding & don't stop it
2. Artificial feeding
 - Mild GE: continue on the same adapted formula
 - Severe G.E: lactose free milk
3. Plenty of fluids.
4. Avoid fat & increase proteins if weaned.

ttt of dehydration

2 methods for correction of dehydration

A. Oral rehydration

- This is the most important single measure in management of G.E
- Composition of oral rehydration solution (ORS)
 - o Na Cl $\Rightarrow$ 3.5 gm
 - o NaHCO₃ $\Rightarrow$ 2.5 gm
 - o KCl $\Rightarrow$ 1.5 gm
 - o Glucose $\Rightarrow$ 20 gm
- ORS is available as packets to be dissolved in 1000 ml water.
- Rehydran $\rightarrow$ 1/5 ORS $\Rightarrow$ dissolve in 200 ml

❖ Methods of administration

1) Cup or spoon

- By the mother slowly & continuously one tea spoonful /1 min.
- Vomiting is not an indication for stopping but if vomiting is severe & persistent we usually revert to IV route



2) Dropper or syringe → may be used .

3) Naso-gastric tube → if the infant is unable to ingest the ORS or refuse it

❖ The amount of ORS

- The baby is given as long as he wishes guided by his thirst
- Usually the deficit is given in 4-6 hrs as follow:
 - a. In mild dehydration : 60-80 ml / kg.
 - b. In moderate dehydration : 80-100ml / kg.
 - c. In severe dehydration : 100-120ml / kg.

❖ Maintenance doses.

- a. 50 ml / one attack of vomiting .
- b. 100 ml /one attack of diarrhea.

B. I.V fluid therapy

i. Initial = 20 ml /kg "1st hour" It is given for treatment of shock .

- It may be given in the form of
 - 1. Blood
 - 2. FFP
 - 3. Plasma expanders
 - 4. Ringer or ringer lactate

The aim of lactate → changed in the liver to bicarbonate → correction of acidosis.

ii. Deficit

- According to the degree of dehydration, the amount of fluid can be estimated from the following table:

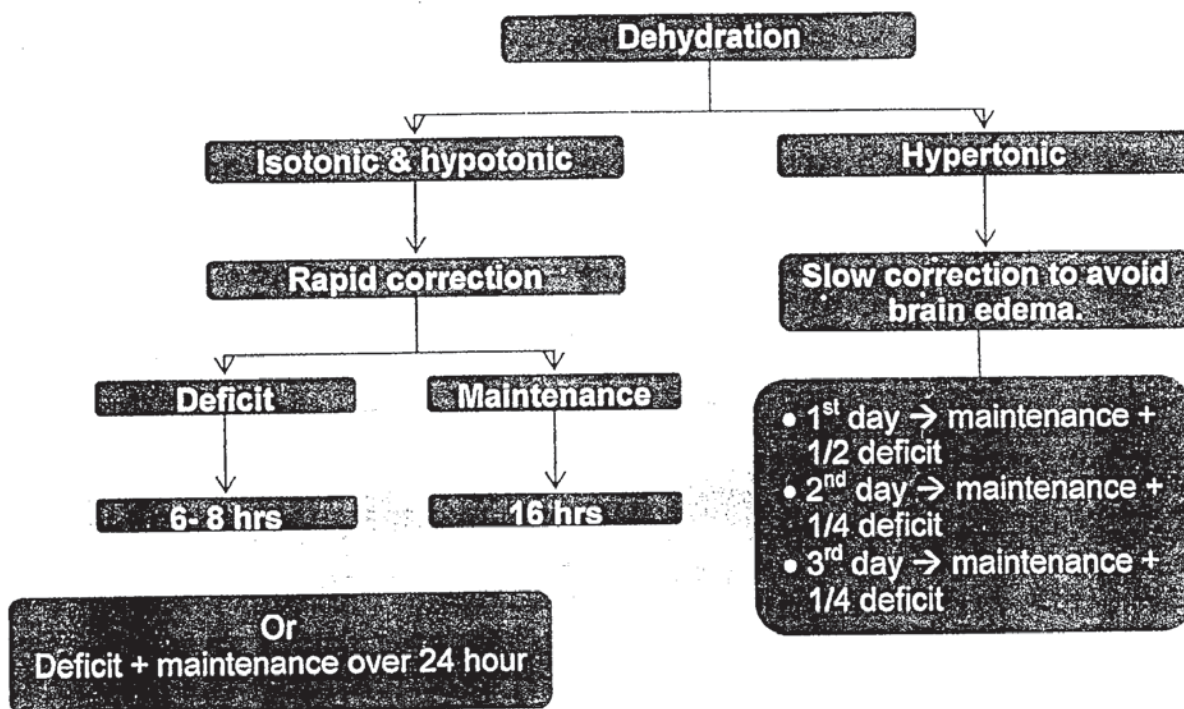
Severity	Infants (Wt < 10 kg)	Children (Wt > 10 kg)
Mild dehydration	50 ml / kg	30 ml / kg
Moderate dehydration	100 ml / kg	60 ml / kg
Severe dehydration	150 ml / kg	90 ml / kg

iii. Maintenance :

- 1st 10kgs → 100 ml / kg
- 2nd 10kgs → 50ml / kg
- >20 kgs → 20 ml / kg Or 2000 ml / m2.

Duration of correction

- 1. Initial ⇒ given in the 1st 1-2 hrs.
- 2. Deficit & maintenance depends on type of dehydration



Type of fluid

- Hypotonic dehydration : hypertonic solution.
- Hypertonic dehydration : Hypotonic solution.
- Isotonic dehydration : Isotonic solution.

Correction of associated electrolytes & acidosis

- Hypokalemia " N. 3.5-4.5 mg/dl" → 3-5 mEq/kg
- Acidosis ⇒ NaHCO₃ according to deficit in blood gases
- Hypocalcaemia ⇒ Ca gluconate 10% solution slowly IV

Symptomatic ttt

1. Diarrhea:

- Anti-motility drugs : are absolutely contraindicated in GE.
- Local antiseptics can destroy the brush border of the intestine & normal bacterial flora.
- Constipating measures may impair the nutrient absorption & may lead to premature stoppage of ORT.

2. Vomiting Anti-emetics & cold drinks.

3. Abdominal distension: Potassium oral & rectal tube.

4. Colic : tincture belladonna

5. Fever: antipyretics.

Dehydration

Definition

- It is a state of -ve water balance
- It's due to *Decrease intake, Excess loss or Both

C/P

1. Acute & marked loss of body weight.
2. Depressed anterior fontanel.
3. Sunken eyes + soft intra-ocular pressure.
4. Dry tongue & mucus membrane.
5. Marked thirst.
6. Loss of skin elasticity (turgor)
7. Diminished urine flow i.e. oliguria & may be anuria.
8. Plus $\Rightarrow$ rapid & weak pulse.
9. Decrease capillary filling time
10. In severe cases $\Rightarrow$ hypotension, shock & collapse $\Rightarrow$ death.
11. Picture of complications e.g. DIC, convulsions and RF.



Degree of dehydration

According to the loss of body weight it is divided into :

A. Mild:

- Loss of up to 5% of body weight
- S&S are mild

B. Moderate :

- Loss of 5-10% of body weight
- S&S are moderate
- Manifestations of peripheral circulatory collapse may be present e.g. pallor, tachycardia & cold extremities.

C. Severe

- Loss of > 10% of body weight
- S&S are severe
- Shock & collapse are usually present

S&S	Mild	Moderate	Severe
Thirst	+	+	+++
Level of consciousness	Alert	Lethargic	Lose, even coma
Capillary refilling	2 sec.	2-4 sec.	>4 sec, cool limbs.
Mucous membranes	Normal	Dry	Very dry
Tears	Normal	Decreased	Absent
Heart rate	Normal	Increased	Markedly increased.
Respiratory rate	Normal	Increased	Rapid & deep.
BP	Normal	Normal	Decreased
Pulse	Normal	Rapid	Weak & rapid
Skin turgor	Normal	Slow	Tenting
Fontanel	Normal	Depressed	Sunken
Eyes	Normal	Sunken	Very sunken
Urine output	Normal	Oliguria	Oliguria or anuria.
	Only thirst	Thirst + signs	Thirst + signs + shock.

Types

	Hypertonic	Isotonic	Hypotonic
Incidence	5 %	80%	15%
Skin			
o Turgor	Fair(±)	Poor ++	Very poor +++
o Temperature	Hot	Cold	Cold
o Color	Gray	Gray	Gray
o Feel	Thickened	Dry	Clammy
Oral m.m.	Very dry	Dry	Moist
Thirst	Severe	Mild	Absent
CNS	Convulsions	Lethargic	Coma
Serum Na	>150 mEq/L	130-150	<130 mEq/L
Osmolarity	>295 mOsm/L	275-295	<275 mOsm/L

Investigations :

1. CBC : Hb & Hct values
2. Serum electrolytes Na, Ca, K
3. Blood gases
4. Renal function tests
5. ECG



N.B.: disturbance of other electrolyte may occur.

Treatment

See G.E.

Electrolyte disorders

Hypokalemia

Serum K < 3.5 mEq / L

Causes

(A) ↑↑↑ Loss

1. Vomiting
2. Diarrhea
3. Fistula

(B) Regulation

1. ↑↑↑ Aldosteron:

- Conn's disease
- Cushing \$.
- Steroid therapy.

2. Renal tubular defect

- Fanconi \$
- Lignac \$
- Light wood \$
- Lowe \$

3. K. Losing diuretic

Lasix

4. Cell regulation

- Alkalosis
- During management of DKA.
- β2 agonist.

C/P

1. Arrhythmia
2. Abdominal distension & constipation.
3. Muscle Tetany

Investigations

- S.K
- Related to etiology
- ECG ⇒ low T wave , Depressed S-T segment, appearance of U-wave.

TTT

- Kcl = 3-5 mEq/Kg/D

Hyperkalemia

Causes

A) ↑↑↑ intake

- Toxic ingestion of K-preparations.
- IV K⁺ administration.
- Rapid infusion of old blood.

(B) Regulation

- ACE-inhibitor e.g. Captopril
- Addison disease
- Spironolactone
- CRF.

(C) Cells

- Acidosis
- DKA before ttt
- Tumor lysis \$

O/P

1. Arrhythmia
2. Abdominal colic
3. Diarrhea
4. Ms weakness

Investigations

S.K > 5.5mEq / L

Ttt

1. Restriction of potassium in diet
2. K- losing diuretics
3. Glucose + insulin
4. β₂ agonist inhalation
5. Dialysis

Hypernatremia

(Na⁺ >155mEq/L)

Causes

A. ↑↑↑ intake of salts:

1. Excess salty food.
2. Ingestion of sea water.
3. Excess saline enema.
4. Hypertonic solution.
5. Excess intake of Na HCO₃ during correction of acidosis.

B. ↑↑↑ loss of water

1. Diarrhea.
2. Vomiting.
3. Excessive sweating.
4. Polyurea : DM, DI.

C. Conn's \$

Hyponatremia

Causes

1. Decrease salt in food
2. Excessive diuretics
3. Excess tape water enema
4. Hypotonic solution
5. Vomiting
6. Diarrhea
7. Psychogenic polydipsia
8. SIADH
9. Hypoaldosteronism

Acidosis

Causes

A. Metabolic

1. Diarrhea
2. CRF
3. Renal tubular defect
 - o Fanconi \$
 - o Lignac \$
 - o Light wood \$
 - o Lowe \$
4. Excess acid production
 - o DKA
 - o Tissue hypoxia

B. Respiratory

- o All causes of respiratory distress

Alkalosis

Causes

A. Metabolic:

1. Vomiting.
2. Iatrogenic due to over correction of acidosis.

B. Respiratory:

1. Hyperventilation
2. Whooping cough.

	PH	HC03	PC02
Metabolic acidosis	↓	↓	↓
Metabolic alkalosis	↑	↑	↑
Respiratory acidosis	↓	↑	↑
Respiratory alkalosis	↑	↓	↓

Viral hepatitis

Etiology

1. Hepatitis A virus
 2. Hepatitis B virus
 3. Non A Non B viruses
 - Hepatitis C
 - Hepatitis E
 4. Hepatitis D: Delta hepatitis
 5. Other viruses e.g. CMV, EBV, rubella, entero-viruses, HIV, Herpes viruses.
- Also : Varicella , mumps, measles, may be complicated by hepatitis.

	Hepatitis A	Hepatitis B
I.P.	4-6 weeks	2-6 months
Age	Commonly in children More severe in adults	Any age
Mode of infection	• Feco-oral • Patient excrete the virus in stool 2 wks before & 1 wk after appearance of jaundice. • No Transplacental or materno-fetal infection. • No carriers	• Commonly parenteral via blood & blood products , even a prick by a contaminated needle may transmit infection. • Transplacental infection may occur • Infected mother transmit the disease to her baby during passage in birth canal

G/P

1. Fever ,either low grade or high grade
2. Pain in the right hypochondrium
3. Dyspepsia
4. Jaundice
5. Tea colored urine & clay colored stool
6. Enlarged tender liver.



Complications of acute hepatitis

1. Acute fulminant hepatitis "I%"
 - more common in cases of hepatitis B when associated with delta agent → It is usually fatal
2. Post hepatitis syndrome
 - Prolonged fatigue, malaise for few months after normalization of liver function tests
 - It is usually disappear spontaneously
3. Chronic hepatitis
 - See-later
4. Cirrhosis
5. Aplastic anemia or nephrosis
6. Hepatoma

Investigations

1. Liver function tests

- SGOT (AST), SGPT (ALT) → markedly ↑↑↑
- Alkaline phosphatase & 5 nucleotidase → moderate ↑↑↑
- S. Bilirubin → ↑↑↑ both direct (early) & indirect (late).

2. Urine

- ↑↑↑ Bilirubin "direct" in the icteric stage

3. Stool: "pale".

4. Hepatitis markers

- To detect hepatitis Ags & Abs.

5. PCR

- HAV-IgM: acute infection by hepatitis A virus.
- HAV-IgG: post infection immunity to hepatitis A virus.
- HBsAg: general marker of infection by B virus.
- HBsAb: document recovery and/or immunity to HBV infection.
- Anti-HBc IgM: marker of acute infection.
- Anti-HBc IgG: past or chronic infection.
- HBeAg: indicates active replication of the virus.
- Anti-HBe: Virus no longer replicating.
- HCV ab: generally used to diagnose HCV infection.

Treatment

A. Uncomplicated cases

→ only supportive ttt

1. Bed rest
2. No restriction of certain elements of diet.

3. If severe vomiting :

- a. IV fluids to avoid dehydration.
- b. Anti-emetics are better avoided "metabolized in the liver"

4. Steroids are not indicated.

5. Interferon is tried for ttt of hepatitis-B (3 mega units 3 times / week for 6-18 months

B. Acute fulminant hepatitis

→ Manage the acute problems, while waiting for restoration of liver function.

1. Encephalopathy

→ reduce blood ammonia level by:

- a. Oral lactulose.
- b. Oral neomycin.
- c. Low protein intake

2. Bleeding:

→ fresh blood or FFP.

Chronic hepatitis

Definition

- A chronic inflammatory reaction in the liver continuing without improvement for more than 6 months

Etiology

1. Persistent viral infection

- o 15% of hepatitis-B
- o 40% of non-A non-B

2. Drugs

- o INH, sulfonamides
- o Methyldopa

3. Auto-immune "lupoid hepatitis"

4. Idiopathic

Types

According to histopathological picture it is divided into:

Chronic persistent hepatitis

1. Benign form
2. Not progressive
3. No development of cirrhosis
4. Excellent prognosis
5. Asymptomatic or non specific C/O
e.g. Anorexia, fatigue, malaise & loss of weight.
6. Vague abdominal pain & slight jaundice.
7. Liver => may be slightly enlarged & not tender.
8. Liver biopsy :
 - o Inflammatory cells are limited to portal area.
 - o Liver architecture is normal
 - o No necrosis of liver cells
 - o No evidence of fibrosis or cirrhosis
9. Laboratory findings
 - o Mild increase of SGOT (AST) & SGPT (ALT).
 - o S. albumin : Normal or slight ↑↑↑.
 - o HBs-Ag +ve in 1/3 of cases.
10. Treatment
No specific ttt is needed
11. Prognosis :
Good, but persistent HBsAg carriers → ↑↑↑ risk of hepto-cellular carcinoma later in life.

B . Chronic active hepatitis

1. Symptoms are mild as chronic persistent hepatitis + fluctuating jaundice.
2. In most patients, HBs Ag is -ve "lupoid type"
3. Hepatosplenomegaly may be present in 50-80%.
4. Other organs involvement → nephritis ,thyroiditis & arthritis.
5. Progress to cirrhosis or liver cell failure.

6. Liver biopsy

- o Liver architecture is distorted
- o Piece-meal necrosis & bridging i.e. necrosis between the portal tract & portal vein.
- o Cirrhosis features may be present.

7. Laboratory findings

- | | |
|---------------------|---|
| a) SGOT & SGPT | → Moderate ↑↑↑ |
| b) S. Bilirubin | → Moderate ↑↑↑ |
| c) Alk. Phosphatase | → N. or slight ↑↑↑ |
| d) S. Albumin | → ↓↓↓ |
| e) PT | → ↑↑↑ |
| f) HBs Ag | → may be +ve |
| g) Other → | - pancytopenia
- LE cells. ANA, Anti-smooth muscle Abs |

8. Treatmenta. Lupoid

- o Prednisolone 30 mg for one week 10-15 mg daily for 2-3 years.
- o Azathioprine may be given with corticosteroids 50-100mg/day.
- o Cyclosporine has been used in patients resistant to corticosteroids.

b. Viral

- o Anti-viral therapy was tried (interferon 3 meg units 3 times/week for 6-18 months).

c. Hepatic transplantation in later stages.9. Prognosis »

75% respond to ttt

Nutritional liver diseases

- These are liver diseases which are caused by nutritional factors

1. KWO - Fatty infiltration
- Nutritional recovery syndrome
- 2- Preterm babies with high protein intake have increased morbidity & mortality
3. Veno-occlusive disease
4. Hemosidrosis associated with protein deficiency + increased iron intake

Veno-Occulsive disease (Infantile liver cirrhosis)

- o Age : 1 - 4 years.
- o Sex : both sexes.

Etiology:

- There is no definite etiological hypothesis.
- It is more common in children living in rural areas with poor dietetic supply. Malnutrition may sensitize the human liver to the effect of toxins derived from herbs.
- Also it may be related to contamination of wheat with pyrolizidine alkaloids.
- Other toxins like aflatoxin produce similar lesions

Pathology

- Small hepatic veins as well as the central sub lobular branches are uniformly thickened described in classical V.O.D.
- Centrilobular necrosis and degeneration with fatty degeneration is present.
- Central fibrosis. follows & proceeds toward non-portal type of cirrhosis.

Clinical picture

A. Acute stage:

1. Sudden painful hepatomegaly.
2. Ascites.
3. Jaundice is inconspicuous.
4. Recover in 6-8 weeks or patients may die of liver cell failure or pass into subacute stage.

B. Subacute stage:

Firm hepatomegaly & recurrent ascites.

- o May follow acute stage directly after a months or may appear de novo.
- o Either subsides or passes into:

C. Chronic stage

Clinically resembles other types of cirrhosis, proved by liver biopsy.

Differential diagnosis

From other causes of cirrhosis & hepatomegaly.

Management

- Low protein & low salt diet.
- Vitamins
- Tapping of Ascites if the patient is distressed.
- Diuretics.
- Plasma & low-salt albumin in some cases.
- Steroids (tried in some cases with good results).
- Antibiotics to prevent infection.
- Omentopexy (to establish anastomosis).
- Hepatic artery ligation to decongest the liver.
- Portocaval anastomosis.

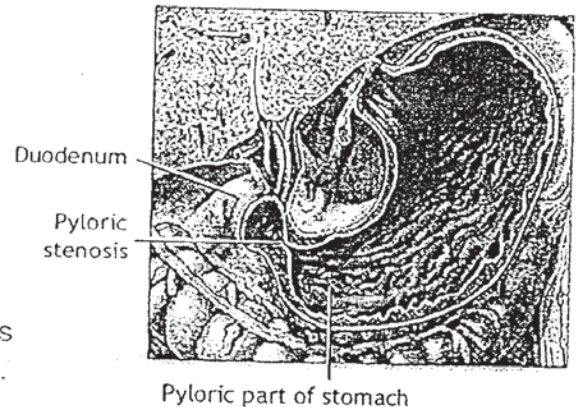
Congenital hypertrophic pyloric stenosis

Etiology

- Hypertrophy & spasm of the circular muscle of the pylorus due to unknown cause

c/p

1. Vomiting :
 - o onset:: usually between 2nd & 4th weeks
 - o character : projectile after each feeding.
2. Constipation.
3. Failure to thrive.
4. Dehydration.
5. Palpable olive green - sized mass in the Rt upper quadrant of the abdomen especially on suckling .



Investigations

- Barium meal → string sign & retained gastric contents!

Treatment

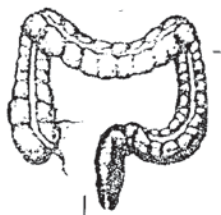
- Pyloromyotomy

Congenital Aganglionic Megacolon "Hirschsprung's Disease"

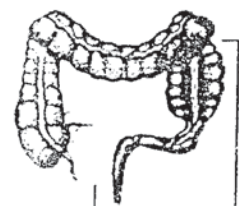
Etiology

- Absence of ganglion cells in the mucosal & muscular layers of the colon
 - o Rectum only "30%"
 - o Rectosigmoid "44%"
 - o All the colon "8%"

NB The denervated segment is narrow ⇒ dilatation of the proximal uninvolved colon



Normal sigmoid colon and rectum



Area affected by Hirschsprung's disease

C/P

1. Constipation alternating with diarrhea "over-flow" is the commonest.
2. Abdominal distension
3. Vomiting may occur if obstruction is severe
4. Failure to thrive
5. Ribbon-like stool due to prolonged stasis in the colon .
6. Distended colon may be felt on abdominal examination
7. On rectal-examination → no feces & narrowing of aganglionic segment.

Investigations

- Barium enema → markedly dilated colon & narrowing of aganglionic segment.

ITT

Colostomy then resection anastomosis

Portal hypertension

Etiology

- According to the site of obstruction of the blood flow, it is classified into :

1. Pre-sinusoidal

A. Infra-hepatic causes :

due to obstruction of portal blood flow before entering the liver

1. Umbilical infection in the neonatal period spread through Para-umbilical v. to the portal vein → thrombosis
2. Congenital narrowing of the portal vein
3. Thrombosis of portal vein due to
 - Polycythemia
 - Dehydration
 - Peritonitis

B. Intra-hepatic causes :

obstruction of the branches of portal vein inside the liver due to:

1. Bilharzial fibrosis
2. Infiltration by → Hodgkin's disease, leukemia & sarcoidosis.

2. Sinusoidal & post-sinusoidal

A. Intra-hepatic causes

obstruction of sinusoids & hepatic venules in the liver due to:

1. Liver cirrhosis
2. Veno-occlusive disease

B. Supra-hepatic causes

- obstruction of the blood flow coming from the liver to Rt ventricle due to:

1. Budd-Chiari syndrome
2. High I.V.C. obstruction
3. Constrictive pericarditis & pericardial effusion.
4. R.V. failure & tricuspid regurge.



A. Symptoms

1. Gastric congestion → dyspepsia & vomiting
2. Intestinal congestion → constipation & abdominal distension
3. Hematemesis & melena → due to rupture varices
4. Abdominal enlargement → due to organomegaly

B. Signs

1. The liver :
 - a. In hepatic causes ⇒ shrunken, firm & has a sharp border.
 - b. In supra-hepatic causes ⇒ enlarged, soft & tender
 - c. In infra-hepatic causes ⇒ normal liver
2. The spleen Enlarged due to:
 - a. Portal hypertension.
 - b. RE hyperplasia
3. Ascites If portal hypertension is associated with hypo-albuminemia
4. Dilatation of the Porto-systemic anastomosis

Investigations

A. Detection of esophageal varices

1. Endoscopy
2. Barium swallow in tendlenberg position.

B. Visualization of the portal system

1. Abdominal sonar
2. CT abdomen.

C. Evaluation of the liver condition

1. Liver function tests.
2. Liver biopsy.



I. TTT of an acute attack of hematemesis:

1. Blood transfusion.
2. Vitamin K administration.
3. H2 blockers (e.g. cimetidine).
4. If the patient is cirrhotic, intestinal sterilization & measures to prevent hepatic encephalopathy (e.g. lactulose, neomycin, frequent enemas & dietary restriction of proteins).
5. Vasoactive drugs, these are used to lower portal pressure both before & as adjuvant to sclerotherapy.
6. Sungestaken-Blackemore tube.
7. Endoscopic sclerotherapy.
8. Endoscopic variceal ligation.
9. Transjugular intrahepatic Porto systemic shunt.
10. Emergency surgery if all measures failed.

II. In-between the attacks:

1. Endoscopic sclerotherapy or ligation to obliterate varices.
2. Surgical Porto systemic shunting.
3. beta adrenergic blockers: it reduce the portal pressure by splanchnic vasoconstriction & reduction of cardiac output. They also reduce hepatic arterial blood flow.

Common causes of Hepatomegaly by age group

Neonates

1. Erythroblastosis fetalis.
2. Idiopathic neonatal hepatitis.
3. Congenital infection (STORCH).
4. Prenatal and postnatal infections (viral & bacterial).
5. Congestive heart failure.
6. Biliary atresia, choledochal cyst & hemangiomas.

Infants

1. PEM.
2. Inborn errors of metabolism (CHO-lipids-proteins & pigments)
3. Cystic fibrosis.-
4. Histiocytosis.
5. Tumours:
 - o 1ry hepatoblastoma & hemangiomas.
 - o 2ry neuroblastoma & Wilm's tumor.
6. Congestive heart failure.

Children

1. PEM.
2. Toxins & drugs.
3. Parasitic infestation,
4. Tumours:
 - o 1ry Leukemia & lymphoma.
 - o 2ry neuroblastoma & Wilm's tumor.
5. Reye's syndrome.

Older children

1. Hepatitis (A,B,C&D)/
2. Chronic active hepatitis.
3. Infectious mononucleosis.
4. Wilson's disease.-
5. Drugs & toxins.
6. Tumours :1ry& 2ry.
7. Parasitic infestations as Bilharziasis.

Complications of liver cirrhosis

1. Ascites.
2. Portal hypertension.
3. Hepatic encephalopathy.
4. Hyper dynamic circulation.
5. Endocrine changes.
6. Impaired hepatic metabolism.
7. Bleeding diathesis.
8. Impaired fat absorption.
9. Susceptibility to infection.
10. Malignant Hepatoma.
11. Gall stone formation.
12. Renal failure.

Differential diagnosis of Ascites in pediatric age group

Types	Mechanism	Pathogenesis	Diagnosis
Transudate	1. Hepatic outflow obstruction	- Heart failure - Constrictive pericarditis - Budd –Chiari -	- Cardiac signs - x-ray - high ascetic protein - biopsy - urinary protein
	2. Hypoproteinemia o Increased loss o Decreased synthesis	- Nephrotic syndrome - Protein loosing enteropathy - Severe malnutrition & malabsorption. - Liver failure. -	- stool Na isotope studies - wasting steatorrhoea - characteristic biopsy - splenic venogram
	3. Intrahepatic and portal obstruction with or without Hypoproteinemia	- Cirrhosis - Portal vein thrombosis (commonly neonatal sepsis)	
Exudates (high protein usually)	1. Infection	- Pyogenic , T.B - Viral e.g. :CMV in neonates	- Culture - Cell count - Ascetic tumor cells and blood
	2. Malignant disease	Wilms , neuroblastoma, carcinoma, hepatoma	- x-ray - associated pleurisy
	3. Intestinal anomalies and obstruction	in neonates e.g. malrotation.	
	4. Polyserositis		
Chylous	Obstruction to lymphatic drainage	- Trauma - Congenital anomalies - Tumor involving cisterna or thoracic duct - ? cirrhosis	- Biopsy of intestinal mucosa - Laparotomy
Biliary	spontaneous perforation of common bile duct	Unknown	Bile stained fluid
Uropathic	? urine transudation	Obstructive uropathy in neonates	

Causes of Cholestasis in Neonates and infants

Surgical

- Biliary atresia.
- Choledochal cyst.
- Cholidocholithiasis.
- Intrahepatic

Neonatal hepatitis

- Idiopathic.
- Viral: CMV, HBV, HCV, EBV, herpes, rubella.
- Bacterial: listeria, syphilis, sepsis, urinary tract infection.

Paucity of intrahepatic bile ducts:

- Syndromic (Allagile).
- Non-syndromic.
- Alpha one antitrypsin deficiency.
- Progressive familial, intrahepatic cholestasis

Metabolic causes:

- Galactosemia.
- Fructosemia.
- Tyrosinemia.
- Neimann-Pick type C.
- Gaucher disease.
- Defects in bile acid synthesis.
- Zellweger syndrome.
- Cystic fibrosis.

Endocrine disorders

- Hypopituitarism
- Diabetes insipidus (Langerhan's cell Histeocytosis).
- Hypothyroidism
- Hypoparathyroidism.

Others

- Chromosomal anomalies: trisomies 21, 18, 13.
- Total parenteral nutrition.
- Neonatal iron storage disease.
- 'Inspissated bile syndrome'.
- Dubin Johnson syndrome.

Hepatomegaly in infants and children

- The liver is the largest organ in the body.
- It constitutes 5% of the total body weight at birth.
- This decreases gradually till it becomes 2% in adults.
- The lower edge of the liver can be felt normally up to 3.5 cm below the right costal margin during the neonatal period. It can then be felt up to 2 cm below the right costal margin in the right mid-clavicular line till 12 years of age.

Concepts of normal liver size is based upon:

The liver span of dullness to percussion i.e. percussing the upper edge (margin of dullness) at 5th intercostal space and the lower edge in right mid-clavicular line and measuring the distance in cm.

The liver span is around 4 - 4.5 cm at birth. It increases gradually till it becomes 7 cm at 3 years and 9 cm at 12 years.

Anatomical abnormalities

1. In some children the right lobe of the liver extends downwards and may be felt as a mass (Reidel's lobe).
2. The liver may be displaced downwards by diaphragm or thoracic organs giving a false impression of Hepatomegaly.
3. Situs inversus totalis: the liver is felt on the left side.



On examining the liver we should notice.

Consistency: firm, soft, hard...

Tenderness

Surface: smooth, irregular.

Border: sharp, rounded.

Masses or bruit (hemangiomas)

Pulsations (tricuspid incompetence)

Mechanisms of Hepatomegaly

1. Increase in the number or size of liver cells
1-Storage 2-Inflammation 3-Infiltration

2. Increase in size of vascular spaces

3. Increase in size of biliary spaces

I. Increase in the number or size of liver cells

1. Storage (inborn errors of metabolism)

The liver plays an important role in the metabolism of proteins, fats, carbohydrates, vitamins and minerals.

Inborn errors of metabolism of carbohydrates:

- Glucose and galactose are metabolized in the liver and the end result is the synthesis of glycogen.
- Glycogen is stored in the liver and its breakdown (glycogenolysis) is facilitated by a series of enzymes.
- Deficiency of such enzymes involved in the synthesis or degradation of glycogen causes abnormal deposition of glycogen in tissues, a condition known as glycogen storage disease.
- Galactose obtained from human breast milk lactose (glucose and galactose) is converted in the liver to glucose. Deficiency of the enzymes responsible for galactose metabolism causes abnormal accumulation of galactose metabolites in tissues, a condition known as Galactosemia.

Glycogen storage disease:

- According to enzyme deficiency more than 12 forms are known.
- According to organ involvement there are 2 forms: muscle and liver.
- Clinical picture in hepatic glycogenosis:

- o Growth retardation and short stature
- o Hypoglycemia
- o Hepatomegaly
- o Some forms present with hepatosplenomegaly and portal hypertension
- o Some present with Cardiomyopathy
- o Some present with myopathy and hypotonia
- o Some present with rickets and renal enlargement

- Diagnosis

- o Fasting blood glucose
- o Liver biopsy to detect the deficient enzyme

- Treatment

- o Continuous supply of glucose to maintain normal blood glucose by day and during night time
- o Liver transplantation in some cases only.



Galactosemia

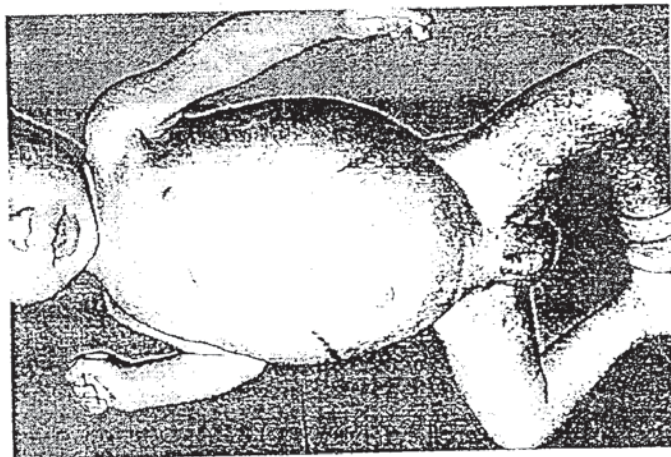
- Clinical picture
 - o Neonatal jaundice
 - o Hypoglycemia
 - o Vomiting and diarrhea
 - o Hepatosplenomegaly
 - o Cirrhosis and portal hypertension
 - o Cataract
 - o Mental retardation if not treated
- Treatment:
 - o Lactose free diet and avoid milk and its products.

Defects in lipid metabolism

- Lipidoses are inherited disorders of lipid metabolism in which abnormal amounts of lipids are stored in various tissues e.g. Gaucher disease, Neimann Pick disease..

Gaucher disease

- it is a multi system Lipidoses
- It is characterized by
 - o Hematological problems due to infiltration of the bone marrow
 - Bleeding tendency (platelet deficiency)
 - Anemia
 - Repeated infections (WBCs deficiency)
 - o Hepatosplenomegaly
 - o Skeletal and bone problems in the form of pain and fractures
 - o Neurological problems in the acute infantile neurogenic type
- It is classified into 3 types according to CNS involvement
 - o Acute infantile (neurogenic)
 - o Chronic adult (non-neurogenic)
 - o Subacute juvenile form
- Diagnosis
 - o Bone marrow aspiration and liver biopsy to detect the abnormal Gaucher cells
 - o Detection of the deficient enzyme
- Treatment
 - o Replacement of the deficient enzyme
 - o Symptomatic treatment (blood transfusion, splenectomy for hypersplenism, analgesics for bone pains)
 - o Bone marrow transplantation.



Inborn errors of proteins and amino acids metabolism

Tyrosinemia

- It is an inborn error of metabolism of the amino acid tyrosine due to deficiency of the enzymes responsible for metabolism resulting in abnormal accumulation of tyrosine and its metabolites.
- It is characterized by
 - o Neonatal Jaundice
 - o Hepatomegaly and liver cirrhosis
 - o Hemorrhage
 - o Liver cell failure in the acute severe type
 - o Renal involvement producing Fanconi syndrome and rickets
 - o Neurological involvement in the severe forms
- Diagnosis
 - o Detection of high levels of tyrosine and its metabolites in serum and urine
 - o Detection of the enzyme deficiency
- Treatment
 - o Restriction of protein and tyrosine in diet
 - o Specific drugs to prevent the formation of toxic tyrosine metabolites (NTBC)
 - o Liver transplantation.

Inborn errors of metabolism of metals and trace elements

e.g. Wilson disease, hemochromatosis

Wilson disease

- it is an inborn error of metabolism of copper resulting in abnormal accumulation of copper in the liver and other organs.
- It is characterized by
 - o Liver disease which presents in any form. It can present as acute hepatitis, acute severe fulminant hepatitis, chronic liver disease...
 - o Corneal affection in the form of gray brown ring around the cornea (Kayser Fleischer ring)
 - o Hemolysis due to affection of red blood cells.
 - o Kidney affection and renal tubular damage leading to Fanconi syndrome
 - o CNS affection (mainly basal ganglia) which appears late in the form of behavior changes, deterioration in school performance, incoordination, tremors and Dysarthria.
- Diagnosis:
 - o High urinary copper
 - o Decrease ceruloplasmin level
 - o Liver biopsy
- Treatment
 - o Copper-free diet,
 - o Copper chelating agents e.g. penicillamine.

Inborn errors of enzymes metabolism

alpha-1 antitrypsin deficiency

- It is characterized by
 - o Neonatal jaundice
 - o Hepatomegaly
 - o Bleeding tendency
 - o Liver cirrhosis and portal hypertension (splenomegaly, Ascites, bleeding esophageal varices and hematemesis)
- Diagnosis:
 - o Low serum alpha-1 antitrypsin level
 - o Protein electrophoresis
- Treatment
 - o Symptomatic e.g. sclerotherapy for esophageal varices
 - o Liver transplantation
 - o Gene therapy in the future

Other inborn errors of metabolism affecting the liver

- Mucopolysaccharidoses.
- Hepatic porphyrias.
- Hypervitaminosis A.
- Fat is stored in the liver causing hepatomegaly in obesity, diabetes mellitus, malnutrition as kwashiorkor and total parenteral alimentation.

Inflammation

A) Hepatocyte enlargement (hepatitis)

- This may be due to
 - a. Viral agents: as acute viral hepatitis A, B, C, D, E. Chronic viral hepatitis B, C, cytomegalovirus, HIV (Human Immunodeficiency Virus), Epstein-Barr virus...
 - b. Bacterial agents: as syphilis (one of STORCH), bacterial abscess, sepsis...
 - c. Parasitic and protozoal: as toxoplasmosis (one STORCH infection or intrauterine infections), Bilharziasis, Fasciola hepatica (transmitted through polluted water and vegetables irrigated with polluted water as lettuce), amoebic hepatitis and amoebic liver abscess.
 - d. Toxic agent: as drugs e.g. INH (used in treatment of T.B), paracetamol ...

B) Kupffer cell enlargement:

- Kupffer cells are phagocytic cells which have an important function to remove bacterial products and antigens reaching the liver through the portal blood.
- Enlargement of Kupffer cells occurs in septicemia and infections, malignancy, granulomatous hepatitis as TB, autoimmune conditions as autoimmune hepatitis and systemic lupus.

Infiltration

- These may be:
 - a) Primary tumors as hepatoblastoma and hepatocellular carcinoma;
 - b) Secondary or metastatic as leukemia, lymphoma, neuroblastoma, Wilms tumor.

II- Increase in size of vascular spaces



- ❖ The venous blood from the liver is drained by 2 hepatic veins which drain
- ❖ into the inferior vena cava to the right atrium of the heart.

This increase in size of vascular spaces may be due to:

- Intrahepatic obstruction to hepatic veins outflow (veno-occlusive disease).
- Hepatic veins or high inferior vena cava obstruction e.g. by thrombosis.
- Congestive heart failure
- Constrictive pericarditis
- Hematopoietic conditions e.g. Thalassemia and sickle cell anemia.

III-Increase in size of biliary spaces

The liver has an important role in production of bile. Bile flows from the liver through bile ductules, bile ducts, common bile duct which opens in the duodenum.

The size of biliary spaces may be increased in the following conditions:

1. Extra-hepatic biliary atresia
2. Congenital hepatic fibrosis (congenital dilatation of intrahepatic bile ducts)
3. Polycystic disease of the liver
4. Choledochal cyst

Evaluation of Children with Hepatomegaly

Physical examination:

Local examination of the liver, splenomegaly, ascites

General examination we should notice

- Growth retardation: by measuring weight, height, height/weight. This growth delay and short stature is noticed in children with hepatomegaly due to
 1. Metabolic causes.
 2. Intrauterine infections.
 3. Children with liver cirrhosis.
- Face: special facial features may be noticed e.g.
 1. Mucopolysaccharidoses doses.
 2. Allagile syndrome.
- Eyes: They should be examined for presence of cataracts e.g. Galactosemia.
 1. Intrauterine infections.
 2. Kayser Fleischer ring in Wilson disease.
- Limbs: They should be examined to detect:
 1. Clubbing in cirrhosis.
 2. Edema in hypoalbuminemia .
 3. Rickets in tyrosinemia...
- Skin: Should be examined for presence of:
 1. Jaundice.
 2. Anemia: Which may be due to:
 - a) Bleeding from esophageal varices.
 - b) Hypersplenism.
 - c) Hemolytic anemia.
 3. Purpura: Which may be due to:
 - a) Intrauterine infections.
 - b) Hypersplenism.
 4. Skin rash.

5. Scratch marks (in cholestasis and biliary obstruction).
6. Palmer Erythema.
7. Spider naevi (in cirrhosis).

▪ Heart: Should be examined for presence of murmurs as:

1. Pulmonary stenosis (in congenital rubella).
2. Ventricular septal defect (in intrauterine infections).

When a child presents with hepatomegaly we should assess:

- ❖ Nature and cause of hepatomegaly.
- ❖ How to monitor response to treatment
- ❖ Severity of the condition
- ❖ Prognosis of the condition.
- ❖ If any specific treatment is required



Investigations

Baseline investigations:

- Complete blood picture
- Urine and stool analysis
- Liver function tests:
 - ❖ Synthetic:
 - Total serum proteins and serum albumin
 - Prothrombin time and partial thromboplastin time
 - ❖ Excretory:
 - Serum ALT (SGPT)
 - Serum AST (SGOT)
 - Total and direct bilirubin
 - Alkaline phosphatase
- Serum glucose and ammonia levels

Second line investigations:

- Abdominal ultrasonography
- Markers of viral hepatitis
- Serology for fascioliasis & Bilharziasis
- Bacterial culture of blood and urine
- Liver biopsy
- Study of intrauterine infections
- Investigations for metabolic diseases
- Endoscopy if needed
- Special radiological studies e.g. CT, MRI, radio isotopic scan

Endocrine

Diabetes mellitus

Definition

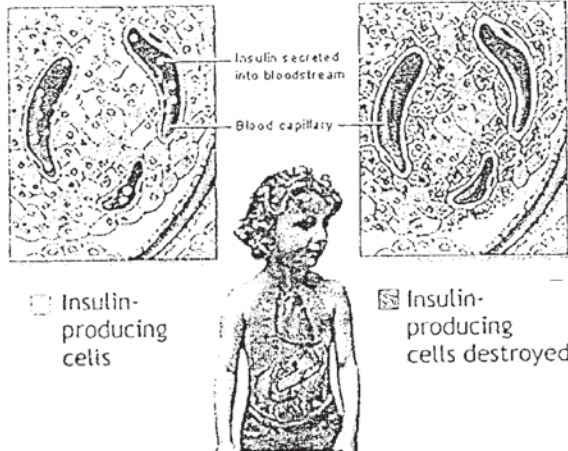
- It is a chronic metabolic disorder caused by relative or absolute deficiency of insulin

The Greek word Diabetes = to Siphon / pass through

Classification

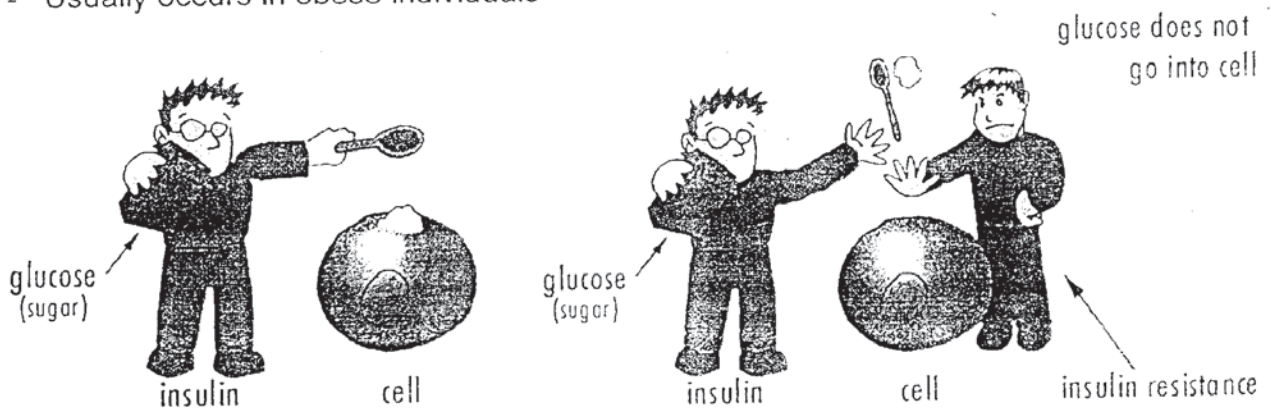
1. Type 1

- IDDM : There is absolute deficiency of insulin → partial , complete



2. Type 2

- NIDDM : here the insulin level is normal but the problem is in the response to insulin .
- Serum concentration of insulin may be normal or moderately depressed
- The onset of the disease occurs after the age of 40 years
- It is rare in childhood and adolescence
- Usually occurs in obese individuals



3. Type 2 in pediatric age :

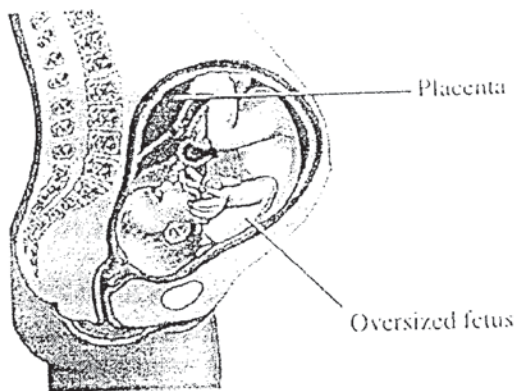
- Maturity onset diabetes of young (MODY) → which like NIDDM but in young age.
- In this type of diabetes there is strong family history of type 2 DM in pattern suggestive of AD inheritance.
- In this type there is no association with HLA , autoimmunity or islet cells Abs.

4. 2ry DM associated with other diseases :

- Pancreatic diseases
- Endocrine diseases : Cushing , $\uparrow$ GH , & steroid therapy
- Genetic diseases : Down , Prader- Willi syndrome
- Insulin receptor abnormalities .

5. Gestational DM

- Occurs in pregnant females.



Etiology of IDDM:

It is not inherited so that family history of DM is not important but it is determined by :

1) Genetic predisposition :

- o A higher incidence of IDDM is observed in association with HLA-DR3 , -DR4 , - B8 & B15.

2) Autoimmune response :

- o Both humoral & cellular mediated response were observed early in the course of disease in most patients with IDDM .
- o Autoimmune response $\rightarrow$ production of Abs either:
 - i. Anti-B cell Abs : " islet cell Abs"
 - ii. Anti-Insulin Abs

3) Environmental factors :

- o Early exposure to cow milk feeding : may be a factor in triggering DM , so DM is lower in breast feed infants .
- o Viruses : " mumps , measles , coxsackie-B2,4&5 " $\rightarrow$ initiate IDDM in genetically predisposed individuals

These infections act by 2 mechanisms :

- i. Autoimmunity
- ii. Change the antigenicity of the cells

Epidemiology of IDDM:

- Sex: both are equally affected
- Age of presentation : 5-7 years & at puberty
- Season : Autumn & Winter
- There is definite increased incidence of diabetes in children with congenital rubella
- Prevalence of IDDM is about 0.2-1.2 in 1000 in Egypt & all over the world .

C/P:

- Asymptomatic : accidentally discovered
- Classic manifestations: polyuria , polydipsia , polyphagia & wt loss .
- 2ry nocturnal enuresis
- Symptoms of complications :
 - 1) Recurrent multiple skin infections e.g monilial vulvo-vaginitis in females:
 - 2) Keto-acidosis in 30 %
 - 3) Hypoglycemia $\rightarrow$ in case of insulin overdose.



polyuria



polydipsia



polyphagia



wt loss

Investigations :

A. For a newly diagnosed patient :

1. Urine : glucosuria $\pm$ Ketone bodies .
2. Fasting blood glucose : $\uparrow \uparrow > 125 \text{ mg/dl}$ "N : $60-110 \text{ mg/dl}$ "
3. Glucose tolerance test "in doubtful cases "
 - The fasting child ingests 1.75 gm / kg glucose in 5 min "maximum = 75 gm total"
 - Blood samples are taken at 0 , 30 , 60 , 120 min . for glucose determination.
 - If 2 hours value & one hour value are more than 200 mg/dl = DM.



Drink glucose



then give blood

4. Serum insulin determination & C-Peptide by radio-immune assay :

- to differentiate between type 1 & 2.

5. Islet cell antibodies (ICA) :

- in 80-90 % of newly diagnosed type 1DM
- The prevalence of these antibodies decrease with the duration of established disease.

6. Anti-insulin antibodies :

- in 30-40 % of newly diagnosed type 1DM.

B. For follow up :

1. Daily blood glucose monitoring (self monitoring)

2. Intermediate monitoring every 2-4 weeks by fructosamine .

3. Long term follow up / 3 months by glycosylated Hb "Hb-A1c " :

- it is formed by an irreversible slow reaction between the N-terminal of beta globin chain of Hb & glucose.
- Since the life span of RBCs is 120 days → so glycosylated Hb is expected to reflect the mean blood glucose concentration in the last 2-3 months.

4. Every year the following are done :

- 1) Blood urea & serum creatinine .
- 2) ALT , AST & Alkaline phosphatase.
- 3) Cholesterol , lipoproteins , HDL & LDL.
- 4) T3,T4 & TSH
- 5) Fundus examination after 5 years of onset of micro albumin in urine.

Complications :

1. ↓↓ immunity

- 1) ↑↑ susceptibility to infections

2. Coma

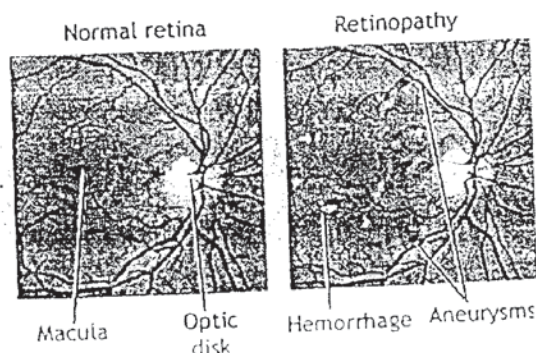
- 1) DKA
- 2) Lactic acidosis
- 3) Hyperosmolar non ketotic
- 4) Hypoglycemia

3. Growth retardation + hepatomegaly

Moriac syndrome

4. Long term complications:

- 1) Neuropathy → sensory > motor & LL > UL.
- 2) Nephropathy
- 3) Retinopathy & cataract
- 4) Cerebrovascular accidents
- 5) Myocardial infarctions.
- 6) Arthropathy.

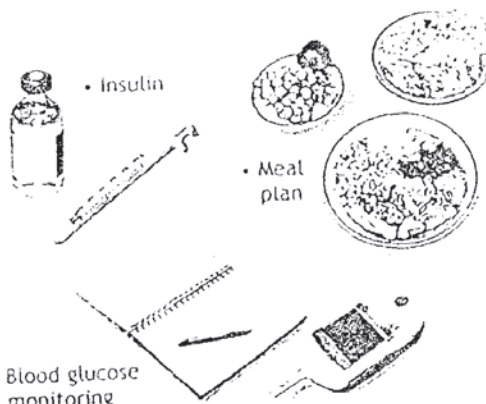


Lines of treatment :

- 1) Diet
- 2) Exercise
- 3) Insulin
- 4) Psychological
- 5) Health education
- 6) Home glucose monitoring

❖ Aims of treatment :

1. Control of hyperglycemia .
2. General health maintenance.
3. Psychological & emotional satisfaction.



Pediatrics

5

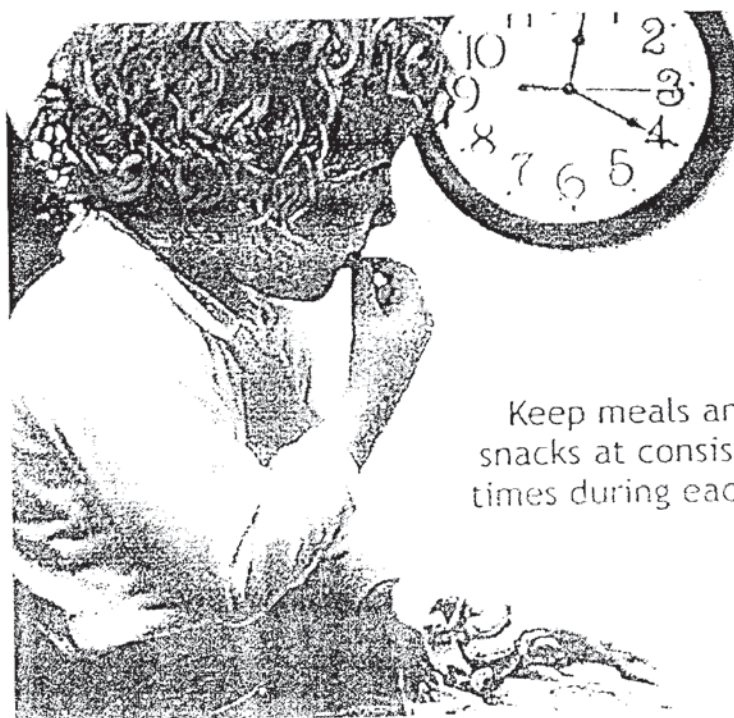
A. Diet

- The major goals of dietetic management are :
 - a. To ensure the pattern of growth and maturation that simulate the pattern of healthy non diabetic children.
 - b. Help the control of wide fluctuation of blood glucose.
- Dietetic management is essential in treatment of DM → usually it is difficult below 5 years.
- Above 5 years :
 1. An adequate total caloric intake should be given to support adequate growth.
The total amount = $100 \times \text{age " years " } + 1000 \text{ calories.}$
 2. Adequate diet should contain :

55 % CHO	30 % Fat	15% Proteins	Vitamins
- Highly refined sugars should be avoided	- Vegetable sources are better. - ↓↓Cholesterol.		- Esp . B complex.

- The total daily caloric intake can be divided as follow " 3 meals + 2-3 mid-meal snacks "
 1. 20% in breakfast
 - ❖ 10 % mid morning snack.
 2. 20% in lunch.
 - ❖ 10% mid afternoon snack
 3. 30 % in dinner.
 - ❖ 10 % evening snack.
- Meals and snacks should be kept at constant time each day.

- **Diet with high fiber contents are useful in control of blood glucose in DM.**
- **Fruits : can be given, but no grapes, mangoes or nuts.**
- **Artificial sweeteners as saccharin & aspartame may be carcinogenic .**



Keep meals and snacks at consistent times during each day

B. Exercise :

- It reduce the amount of required insulin.
- However the caloric contents of snacks should be increased for fear of hypoglycemia .
- It should be :
 1. Non- competitive : due to $\uparrow\uparrow$ epinephrine secretion in competition .
 2. Not causing stress or fatigue .
 3. If hypoglycemia occurs $\rightarrow$ orange juice or sugars should be available.



❖ Advantages of exercise :

1. $\downarrow\downarrow$ coronary heart disease.
2. Weight control.
3. Psychological satisfaction.
4. $\downarrow\downarrow$ insulin requirement ; the dose of insulin may be reduced 10- 15 % on the day of exercise .

C. Insulin therapy :

A. Insulin structure :

- Insulin is small protein (MWT is about 5800) made of 2 polypeptide chain :
 - o A chain : 21 a.a.
 - o B chain : 30 a.a.
- Human insulin differs from porcine only at one amino acid at position No. 30 of (B) chain.
- Bovine insulin differ at two other sites amino acid 8 & 10 of the (A) chain.

B. Types of available insulin :

❖ Sources:

- 1) Pork
- 2) Beef
- 3) Human insulin

a. Regular or crystalline insulin.

- o Onset : 1/3 – 1 hour .
- o Peak : 2-4 hours.
- o Duration : 6- 8 hours.

b. Intermediate onset & duration :

- o Onset : 2 hours .
- o Peak : 4-12 hours.
- o Duration : 24 hours .
- o e.g : NPH , lente , mixtard , monotard .

c. Delayed onset & long duration :

- o these are not used in children below 6 years as they may cause night hypoglycemia , convulsions or death e.g. Insulin Glargin.

C. Regimens of insulin therapy :

- Two types of insulin regimens in routine use :
 - 1) Conventional therapy : (twice daily) .
 - 2) Intensive therapy (Multiple dose regimen)

Pediatrics

1) Conventional therapy :

- Below 10 years .
 - Pregnant DM
 - Newly diagnosed who retained endogenous insulin secretion .
- Usually a combination of short + intermediate duration of insulin is used .
 - The total daily dose of insulin = $1/2 - 1$ unit / kg.

2/3 morning		1/3 evening	
2/3 NPH	1/3 crystalline	2/3 NPH	1/3 crystalline.

2) Intensive insulin therapy :

- Above 10 years .
 - Labile (brittle DM).
 - With rapid advancing tissue damage requiring near perfect glycemic control .
- 3-5 insulin injections / day .
 - Short acting before each meal & intermediate or long acting before bed time

D. Recent lines :

- Insulin pump : → allow better control of blood glucose.
- Pancreatic transplantation .
- Trials therapy in newly diagnosed IDDM :

a. Immune-modulator :

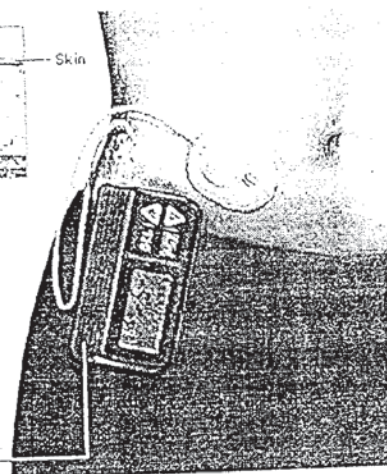
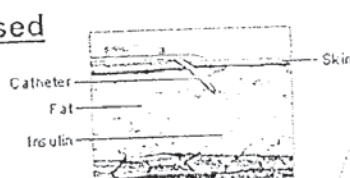
- IVIG.
- Plasmapheresis.
- Interferon.
- Thymic hormone.
- Levamisole.

b. Immune-suppressants:

- Cyclosporine + Azathioprine.

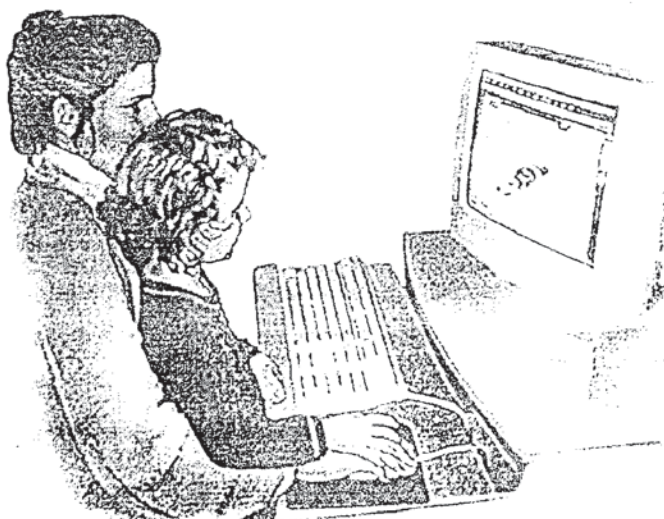
E. Complications of insulin therapy :

- Hypoglycemia
- Lipidystrophy at the site of injection.
- Allergy & antibody formation .



D. Psychological management in IDDM:

- Patients need continuous balance between love & limits .
- Camps for diabetics to provide an enjoyable reaction , freedom & independence.



D.K.A.

- Keto-acidosis may be the initial presentation in 30 % of cases of IDDM.

Etiology :

1. Missing doses of insulin.
2. Low dose of insulin .
3. Infection.
4. Stress.

G/P :

1. Dehydration + Polyuria.
2. Metabolic acidosis: deep rapid respiration " Kausmol"
3. Cerebral deterioration ending in coma.
4. Acetone breathing.
5. Abdominal pain or rigidity may mimic acute appendicitis or pancreatitis.

Investigations :

1. Blood glucose > 300 mg/dl.
2. Ketonemia > 3 mMol/L (↑↑ B hydroxybutyrate & alpha acetoacetate)
3. Metabolic acidosis :
 - PH < 7.30
 - HCO₃ < 15 mEq /L
4. Additional laboratory investigations
 - K + ECG → for hyperkalemia
 - If sepsis is suspected CBC , blood culture , urine culture .

Treatment :

It is a hospital emergency . the major lines of treatment are :

1. Correction of dehydration & electrolyte disturbance.
2. Correction of hyperglycemia.
3. Correction of acidosis.
4. Treatment of precipitating factors e.g infection.

A. Correction of dehydration :

Amount of fluid needed :

- 1st hour → 500 ml / m².
- Next 2 hours → 500 ml / m².
- Next 9 hours → 100 ml / kg.
- Next 24 hours → 2000 ml / m².

OR :

- The total amount of fluid calculated in 36 hours can be given as follow :
 - 50-60 % in the first 12 hour
 - The remaining amount 40-50 % in the remaining 24 hours.

This policy aims at :

- Rapid refilling of circulation as management of shock .
- Then we reduce fluids to 1/2 to prevent encephalopathy , after which idiogenic osmoles disappear so that we can ↓↓ the rate.

Why oral intake is contraindicated before 36 hours ??

1. To rest the stomach " irritated by K.B "
2. Oral fluid modulator GIT hormones

B. Types of fluids :

- Start with normal saline.
- Once blood glucose $\rightarrow \leq 300$ mg % $\rightarrow$ give glucose 5% in normal saline.

C. Treatment of hyprglycemia :

- By insulin therapy as follows :
 - 1) Short therapy : 0.1 U / Kg IV shot.
 - 2) Then 0.1 U / Kg / Hr.
 - 3) When blood glucose reach ≤ 300 mg % $\rightarrow$ 0.05 u/kg/hr.

D. Treatment of acidosis :

- If PH $> 7.2 \rightarrow$ no correction
- If PH $< 7.2 \rightarrow$ correction according to bicarbonate deficit in blood gases.

E. Treatment of infection :

- Broad spectrum antibiotics.

Complication during treatment :

1. Hypokalemia or hyperkalemia .
2. Hypoglycemia
3. Hypocalcemia
4. Over whelming infection.
5. Irreversible fatal cerebral edema or Hge.

D.D of DKA :

1. From other causes of coma as non-ketotic & hypoglycemic coma.
2. Complicated gastroenteritis
3. Uremia
4. Lactic acidosis.
5. Salicylate intoxication.
6. Encephalitis & intra-cranial lesions.
7. Pneumonia.

Post acidotic phase or transition period for establishment of metabolic control

- ❖ DKA usually corrected within 36-48 hours . then at the transition stage SC crystalline insulin are begun at a dose of 0.1-0.25 U/Kg every 6-8 hours, before meals with simultaneous monitoring of the blood glucose & adjustment of insulin dose for 1-2 days .
- ❖ The aim of therapy during the transitional period are to treat any recognized precipitating cause of DKA such as infection , to stabilize the patient metabolic control by adjusting the insulin dose .

Dwarfism

- Normal growth is the expression of :
 1. Hormonal factors
 2. Environmental factors
 3. Nutritional factors
 4. Genetic factors

Types :

A. Proportionate :

- Whole body is proportionately affected e.g. : pituitary dwarfism.

B. Disproportionate

- Lower segment is more affected than upper segment & span is more affected than height .

Genetic height potential :

- It is the expected adult height in normal persons .
- It can be calculated from the mid-parental height " height of father + height of mother / 2 " as follows:
 - 1) Add 6.5 cm to mid-parental height in case of boys.
 - 2) Subtract 6.5 cm from mid-parental height in case of girls.
 - 3) The genetic height potential is ± 8 cm

Causes of dwarfism :

❖ Primary disorders

i. Disproportionate short stature :

- Skeletal causes :
 - 1) Achondroplasia : short limbs & normal trunk.
 - 2) Osteogenesis imperfecta : fragile bones $\rightarrow$ multiple fractures $\rightarrow$ mal- union dwarfism .
 - 3) Pott's disease of spine.
- Congenital error of metabolism:
 - 1) MPS.
 - 2) Rickets .

ii. Dysmorphic features :

- Syndromes with chromosomal aberrations :
 - 1) Turner's syndrome .
 - 2) Down syndrome.
- Syndromes without chromosomal aberrations :
 - 1) Silver Russell syndrome.
 - 2) Noonan syndrome.

❖ Secondary disorders :

i. Nutritional diseases and malabsorption :

- 1) Poor weight gain usually occurs before short stature is noticed .
- 2) Characteristic features of malnutrition .

ii. Endocrinal diseases :

1. Cretinism
 - Disproportionate dwarfism
 - Characteristic features of cretinism
2. Pituitary dwarfism
 - Due to $\downarrow\downarrow$ GH.
 - Proportionate dwarfism
3. Laron syndrome:
 - Due to $\downarrow\downarrow$ somatomedins (IGFs).
4. Froehlich syndrome:
 - Trunkal obesity
 - Hypogonadism
 - Genu-valgus.
5. Precocious puberty
 - Premature fusion of epiphysis .
6. Cushing disease or syndrome.
7. Diabetes mellitus .
8. Pseudo-hypoparathyroidism.

iii. Chronic illness.

1. Severe heart disease.
2. Chronic infection & toxemia.
3. Liver cirrhosis & lipid storage disease.
4. Chronic nephritis & DM.

iv. Iatrogenic short stature

- Chronic steroid therapy.

v. Psychogenic short stature:

- Emotional deprivation.
- Anorexia nervosa.

❖ Normal variant or idiopathic

i. Familial :

- The patient has short parents.
- There is normal growth velocity & normal bone age.

ii. Constitutional :

- Here , there is normal growth velocity.
- Bone age & puberty are delayed.
- Typically there are :
 - 1) Normal at birth ; with normal growth till 6 months.
 - 2) Then : growth becomes very slow till 2 years age " <5th percentile ".
 - 3) Then there is normal growth velocity " growth curve is parallel to that of 5th percentile "
 - 4) Growth continues for a longer time than normal " due to delayed puberty " →so height becomes normal again .
 - 5) Family history is usually +ve.

Investigations:

1. CBC :

- Chronic anemia , infection.

2. ESR :

- Collagen diseases.
- Chronic infection as T.B .

3. Urine analysis :

- Pyelonephritis.
 - Glomerulo-nephritis.
 - Renal tubular disease.
- e.g : Fanconi syndrome , lignac syndrome , Lowe syndrome.

4. Stool :

- Parasitic infestation.
- Occult blood – undigested food.

5. Renal function test.

6. Karyotyping.

7. Thyroid functions.

8. GH & somatomedins

Treatment:

Depends on the cause:

1. Familial → no treatment.
2. Constitutional → re assurance .
3. Cretinism → see later.
4. Pituitary dwarfism → GH.
5. Turner syndrome → GH + sex hormone.
6. Treatment of chronic disease

Growth hormone

- GH is an anterior pituitary hormone.
- It's release is controlled by 2 hormones , GHRH which is stimulatory & somatostatin which is inhibitory.
- It induce linear growth directly & indirectly by inducing insulin like growth factor 1 (IGF-1) secretion by the liver.

Causes of GH deficiency:

1. Birth trauma.....Ichge in the pituitary fossa.
2. Hereditary.....due to genetic defect.
3. Congenital developmental anomalies.
4. Inflammatory.
5. Cranial irradiation.
6. Craniopharyngioma.
7. Histeocytosis.
8. Maternal deprivation.

Investigations:

- 1) GH assessment: < 10 ng / ml is diagnostic.
- 2) Provocation test : by insulin or clonidine.

Treatment:

Recombinant GH : 15-20 IU / m² / week ,divided into 3-6 doses SC at bedtime.

Tall stature

Definition:

> 95th percentile or > 2 SD above the mean for age & sex.

Causes:

1. Familial.
2. Endocrinal.
 - Pituitary gigantism.
 - Hypogonadism.
 - Precocious puberty in 1ry school.
3. Chromosomal:
 - XXY.
 - XYY.
 - XXX.
4. Others:
 - Marfan S.
 - Homocystinuria.
 - Cerebral gigantism. (SOTO S).
 - Simple obesity.

Cretinism

Definition:

- It is congenital hypothyroidism i.e: occurring since birth.

Causes:**A. Permanent:**

1. Congenital absence or hypoplasia of thyroid gland.
2. Congenital defect.
 - TSH receptor defect.
 - Iodine trapping defect.
 - Organification defect.
 - Iodotyrosine deiodinase deficiency.
 - Thyroglobulin defect.

↓↓ thyroxin level → ↑↑ TSH ⇒ Goiter.
3. Endemic cretinism → due to iodine deficiency.
4. ↑↑ use of anti-thyroid drugs or radio-active iodine during pregnancy.
5. 2ry hypothyroidism → hypopituitarism.
6. Tertiary hypothyroidism → hypothalamic function.

B. Transient :

1. Maternal ingestion of goitrogenic substances
 - o Iodine (cough expectorant)
 - o Anti-thyroid drugs.
2. Maternal iodine deficiency .
3. Maternal transfer of TSH receptor blocking antibodies.
4. Neonatal use of iodine antiseptics.



A. General features :

1. Face:
 - 1) Low anterior hair line.
 - 2) Puffy eye lids.
 - 3) Depressed nasal bridge.
 - 4) Big lips.
 - 5) Large protruded tongue.
 - 6) Delayed dentition.
2. Hands:
 - 1) Short tapering fingers.
 - 2) Square shaped.
 - 3) Dorsal pad of fat.
3. Disproportionate dwarfism:
The height is more than the span.
4. Delayed walking & waddling gait.
Due to dysgenesis of the femur head muscle weakness.
5. Subnormal body temperature.



B. Skin manifestations:

1. Dry, rough , scaly, cold skin.
2. Hair is scanty , coarse & brittle.
3. Deposition of S.C myxoedematous tissue particularly on the dorsum of hands , face & subclavian regions.

C. Nervous manifestations :

1. MR :
 - o Delayed motor milestones.
 - o Delayed talking.
 - o Delayed sphincteric control.
2. Hoarse cry

D. Cardiovascular manifestations :

1. Bradycardia.
2. ECG → low voltage.

E. Muscle weakness:

1. Pot belly abdomen.
2. Umbilical hernia.
3. Constipation.

F. Early manifestations:

1. Over weight baby .
2. Prolonged physiological jaundice.
3. The baby sleeps much , cries little & feeds little.
4. Delayed closure of posterior fontanel.

5. Abdominal distention, constipation & umbilical hernia.
6. Hoarse cry.

N.B : Examination of the neck is very important to exclude thyroid swelling.

Investigations:

A. Hormonal assay :

1. In 1ry hypothyroidism :
 - o $\downarrow\downarrow$ T3, T4 " N:4-9 ug/dl"
 - o $\uparrow\uparrow$ TSH " N:2-10 U/L"
2. In 2ry & 3ry hypothyroidism :
 - o TSH is low

How to differentiate between them ?? by TRH stimulation test :

- a) If $\rightarrow \uparrow\uparrow$ TSH = tertiary hypothyroidism.
- b) If $\rightarrow$ no response = 2ry hypothyroidism.

B. Serum cholesterol level $\rightarrow \uparrow\uparrow\uparrow$

C. ECG $\rightarrow$ low voltage + sinus bradycardia.

D. X-Ray :

1. Delayed bone age.
 - o At birth $\rightarrow$ absent distal femoral epiphysis.
 - o Later $\rightarrow$ delayed appearance of carpal bone.
2. Epiphyseal dysgenesis:
 - o Affecting head of femur & humerus.
3. Beaking of T12 & L1,2 vertebrae.
4. Intra-suture bone in skull $\rightarrow$ Wormian bone.

E. Others :

1. Thyroid scan.
2. Thyroid biopsy.
3. Thyroid antibodies.

D.D:

- From other causes of mental & growth retardation e.g. : Mongol & MPS.

Treatment:

- Hormonal replacement therapy for life :

L-thyroxin tab $\rightarrow$ 4 ug / kg / d then gradual increase the dose according to clinical & laboratory response.

- 1) GIT $\rightarrow$ constipation or diarrhea.
- 2) Pulse $\rightarrow \downarrow\downarrow$ or $\uparrow\uparrow$
- 3) Appetite
- 4) Growth in weight and height.

N.B Pendred syndrome:
deafness, goiter.

Prognosis :

- The prognosis depends upon:
 - a. Early diagnosis and treatment.
 - b. Severity of thyroid hormone deficiency.
- 1. Cases treated before 3 months $\rightarrow$ very good prognosis for mentality.
- 2. 3-6 months $\rightarrow$??
- 3. After 6 months $\rightarrow$ poor mentality.

Juvenile Myxedema

- It is acquired hypothyroidism during childhood.

Etiology :

- 1) Autoimmune thyroiditis.
- 2) Surgical removal of thyroid gland.
- 3) Ingestion of goitrogenic substances.
- 4) Endemic iodine deficiency.
- 5) 2ry or 3ry due to tumor , trauma , infection or irradiation.

Treatment:

- As cretinism.

Glomerular Disorders

Pathogenesis of Immune-mediated Glomerulopathy

Hypersensitivity Reactions

- Occurring within the kidney (type II cytotoxic).
- Circulating antibodies + antigens at the glomerular basement membrane (GBM) in 5% of cases of glomerulopathy.
- Example:
 - Good pasture's syndrome.
 - Rapidly progressive glomerulonephritis.

Immune-complex Disease

⇒ Type III hypersensitivity:

- Antigen (exogenous or endogenous) + antibody + complement → **initiate inflammatory process in the kidney.**
- Renal biopsy → **Immune complex deposits** in the kidney.
- Examples:

Antigens	Clinical Condition
<u>Exogenous:</u> • Drugs – toxoid. • Foreign serum.	• Serum sickness. • Glomerulonephritis.
<u>Bacterial infections:</u> • Streptococci. • Staphylococci. • Salmonella. • Syphilis.	• Post-streptococcal GN. • Typhoid fever. • Membranous nephropathy.
<u>Parasitic infections:</u> • Malaria. • Bilharziasis. • Toxoplasmosis.	• Nephrotic syndrome.
<u>Viral infections:</u> • Hepatitis B. • EB virus.	• Viral hepatitis + rapidly progressive GN.
<u>Endogenous:</u> • Nuclear antigens. • Tumor antigens. • Renal tubular antigens.	• SLE nephropathy. • Hodgkin's + GN.

Initiation of Cellular Immunity by GBM antigens

Example: chronic GN.

Clinical Presentations Of Glomerular disorders

1. Nephrotic syndrome.
2. Acute GN.
3. Nephritic Nephrotic.
4. IgA nephritis.
5. Acute renal failure (ARF).
6. Chronic renal failure (CRF).
7. Recurrent or persistent hematuria.
8. Asymptomatic proteinuria.
9. Rapidly progressive GN (with crescent)
10. Hemolytic uremic syndrome (HUS).

Nephrotic Syndrome

Definition

- **It is a clinical syndrome characterized by:**

- 1- Heavy proteinuria > 2 gm/24hrs.
- 2- Hypoproteinemia.
- 3- Marked generalized edema.
- 4- $\pm$ Hypercholesterolemia.

Etiology

1ry	2ry
1. Minimal change GN. 2. Cong. GN. 3. Membranous GN. 4. Membrano-proliferative. GN. 5. Rapidly progressive GN. 6. Focal glomerulosclerosis.	1. SLE. 2. DM. 3. Henoch schonlein purpura. 4. Sickle nephropathy. 5. Malignancies e.g. lymphoma. 6. Gold & D-penicillamine. 7. Malaria & S. Mansoni.

→ auto Ab against
sialopph.

Minimal Change GN

Etiology

↳ only pathology in 1 kid. is fusion of foot processes.

- Loss of - ve charge of sialoproteins which are present in the wall of fenestra of basement membrane due to immunologic disorders (T-cell dysfunction) so, it is improved by measles infection. Ⓚ Bad.

Incidence

1. > 70% (commonest cause of nephritic syndrome in pediatrics).
2. Age: 2-7 Years (it can be < 1 year).
3. Sex: ♂ : ♀ = 2 : 1.

Pediatrics

3

Clinical Picture

1. Massive Generalized Edema:

- Puffy eye lids.
- Pleural effusion
- Pericardial effusion → *periCard. الـسوائل*
- Ascites.
- Scrotal edema
- Lower limb edema.



Puffy eye lids

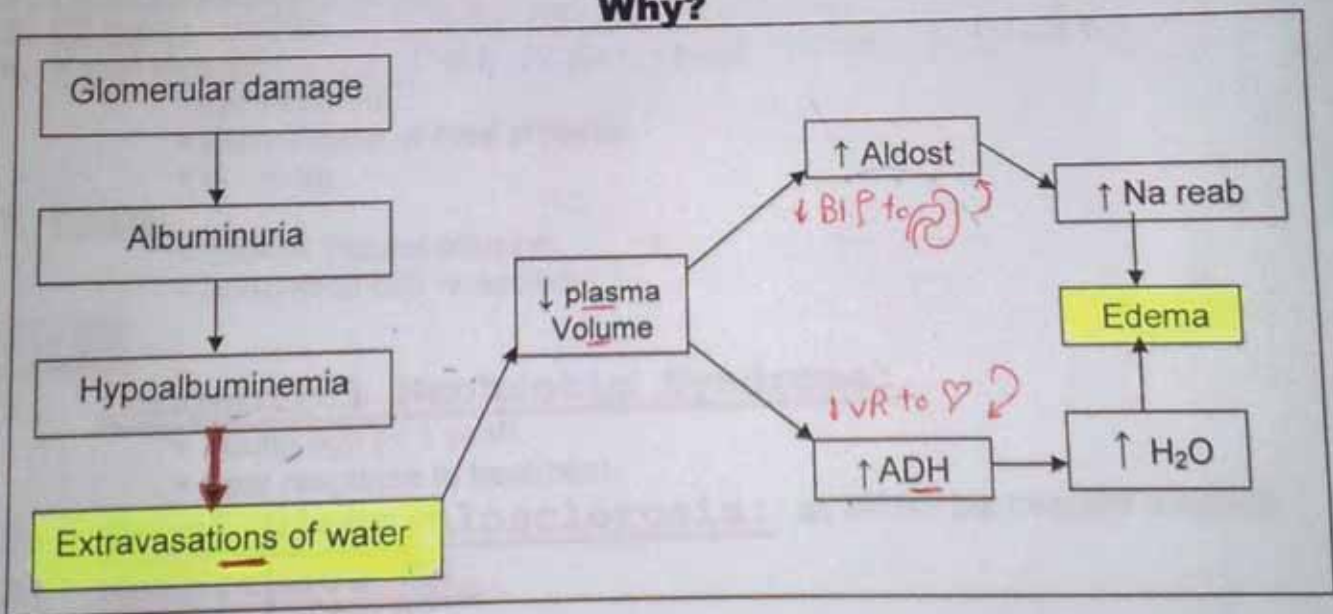


Ascites



Scrotal edema

Why?



2. No:

- Oliguria
- Hypertension
- Hematuria

3. Associated Complications:

A. ↑↑ Tendency for Infection due to:

1. Loss of IgG.
2. Loss of tuftsin. *acts against capsulated org. " phagocytic function "*
3. Immunosuppressive drugs used in treatment.
4. Presence of edema or ascites. *" wetness - stasis "*

B. **↑↑ Risk of Thrombosis due to:**

- ④ **↑ Blood Viscosity**
1. Hemo-concentration due to edema & use of diuretics., *Steroid d.t Poly Gythemia.*
 2. Hyper-cholesterolemia.
 3. Loss of antithrombin III, protein C&S in urine. ↓
 4. ↑↑↑ release of certain coagulation factors. ↑

Investigations1. **Urine analysis:**

- Heavy proteinuria (> 2gm /24hrs urine).
- Mainly selective proteinuria (albumin, transferrin, IgG).

2. **↓↓ Total Protein & Serum Albumin < 2.5 gm/dl.**

- Normal level of protein = 6-8 gm% & albumin = 4.5-5 gm %).

▪ Hypoproteinemia is due to:

- 2ry to excess urinary loss.

- Loss of serum protein into the GIT. *edema in mm of GIT*

- ⑤ **↑↑ rate of albumin catabolism.** *congestion*

3. **Serum Cholesterol:**

- > 300 mg/dl (normal level = 150-250 mg %).

▪ Hyperlipidemia is due to:

- **↑↑** lipoprotein synthesis by the liver to correct the decreased osmotic pressure 2ry to Hypoalbuminemia.

- **↓↓** destruction of cholesterol by the liver due to **↓↓** lipoprotein lipase enzyme.

4. **Renal functions:** normal.5. **C3 level:** normal.6. **Renal biopsy:**

- LM = Normal.
- EM = Fusion of foot process.
- IF = -ve.

7. **Others:**

- CXR → Pleural effusion.
- Abdominal U/S → ascites.

DD

1. **Congenital Nephrotic Syndrome:**

- Young age (< 1 year).
- Poor response to treatment.

2. **Focal Glomerulosclerosis:** as MCNS but frequent relapses.3. **Membranous GN:**

- Age > 10 years.
- Non-selective proteinuria.
- Poor response to treatment.

4. **Membrano-proliferative GN:**

- Age > 10 years.
- **↓↓↓** C3.
- Hematuria.
- Hypertension.
- Azotemia.

5. **Secondary glomerulopathy with systemic diseases:**

- DM & SLE.

Treatment

1. Rest:

Because exercise will lead to

1. ↑↑ proteinuria ↑ $\uparrow$ R. upright position → ↑ Renal Bl. flow → GFR, ↓ urea.
2. ↑↑ catabolism of protein. "↑ BMR".

2. Diet:

1. High albumin containing food e.g. egg - white.
2. Low salt diet. → as Aldosterone is ↑ + salt → aggravated edema.
3. Low fat.
4. ↑↑ CHO. → يحرقها بدل البروتين

3. Diuretics:

Usually given alone in the 1st two weeks without steroids because:-

1. Spontaneous remission may occur.
2. ↓↓ Ascites → ↑↑ renal perfusion. → ↓ Compression on Kidney.
3. ↓↓ Edema → so we can reach the actual body weight.
4. ↓↓ Tissue edema → enhance response to steroids.
5. During these 2 ws we can exclude any infections esp. T.B.

One of the following drugs can be used

1. Lasix (furosemide) → 1-3 mg / kg + K syrup
2. Aldacton (spironolactone) → 1-3 mg / kg.
3. Osmotic diuretics → Mannitol 20% IV drip over 30 min followed by IV Lasix 1 mg / kg.
4. Salt free albumin followed by lasix: To ⊖ hypervolemia, ⊖ congestive HF.

The role of salt free albumin in treatment is:

- Strong diuretics in presence of massive edema.
- It compensates ↑↑↑ level of lipoproteins. ↑↑↑ level of big molecular weight proteins, ↑↑↑ level of coagulation factors.

4. Drugs:

- Prednisone 2 mg / kg / D (max. 60 mg / m² / D).
- Cyclophosphamide (Endoxan): 1-2 mg / kg / D for 6 ws.
- Chlorambucil in frequent relapses 0.2-0.4 mg / kg for 3 months.
- Indomethacin (Indocid) in resistant cases.
- Azathioprine (Imuran).
- Levamisole (Ketrax): 2.5 mg / kg twice / week.
- Anticoagulants in cases of membrano-proliferative type or in presence of thrombosis.
- Cyclosporine A (5 mg / kg) for 6 months in resistant cases or presence of side effects of steroids.

Treatment

A. Treatment of 1st Attack:

- The aim of Treatment is to ↓↓ protein excretion in urine.
- Usually we start by prednisone tablets 2 mg/kg/D for 10-14 days after complete absence of proteinuria, and then start gradual tapering.
- If proteinuria persists after one month, it is an indication for renal biopsy.
- According to renal biopsy:
 - ⇒ Minimal change NS: give prednisone for another one month.
 - ⇒ Focal glomerulosclerosis: Intermittent prednisone + alkylating agents for 3 months.
 - ⇒ Membranous nephropathy: no Treatment (10% pass to chronic renal failure).
 - ⇒ Membrano-proliferative GN: intermittent prednisone therapy + anticoagulant + Antimetabolite (azathioprine).

تحتوي على
prednisone +
alkylating agents

3-6

Bad Prog.

- 30 % of patients who respond to steroids will not have relapse & 70 % will relapse for 1-3 times/ year.

B. Treatment of Relapse:

- Start with prednisone as Treatment of 1st attack, then give steroids one single dose in the early morning every other day for 6 months.

C. Treatment of Frequent Relapses:

- Intermittent prednisone + daily Chlorambucil or Cyclophosphamide for 6 weeks to 3 months.

Nephrotic Syndrome in the 1st Year of Life

1. Infantile micro cystic disease (congenital nephrosis):

- Autosomal recessive disorder.
- Clinically presented by generalized edema & highly selective proteinuria since birth.
- Renal biopsy: cystic dilatation of proximal renal tubules.
- Can be diagnosed intra-uterine by detection of $\uparrow\uparrow$ α -fetoprotein in amniotic fluid at 14-16 weeks.
- The prognosis is usually fatal ending in renal failure.

2. Membranous nephropathy of congenital syphilis:

- Onset at 6 months.
- Renal biopsy: membranous nephropathy immune deposits.
- Antisyphilitic treatment is curative.

3. Minimal change Nephrotic syndrome:

Can occur at the age of 6 months.

4. Focal glomerulosclerosis.

5. Idiopathic membranous glomerulopathy:

- Treated by intermittent course of steroids for 6 months.

6. Mercury poisoning.

7. Congenital toxoplasmosis: treated by daraprim 2 mg/ kg.

8. Nail-patella syndrome:

- Nephrotic syndrome + Absence of patella + Atrophy of nails.

9. Nephroblastoma: with or without abnormal genitalia.

10. Hemolytic uremic syndrome:

- Autoimmune disease $\Rightarrow$ Acute hemolytic anemia + massive nephritis + thrombocytopenia + microangiopathy.
- It is a serious disease usually preceded by a short period of gastroenteritis or respiratory tract infection. Then after 2 days the infant develops sudden pallor, Oliguria or anuria, toxemia & bleeding tendency in the form of petichae or purpura.
- It is an example of consumption coagulopathy & characteristic RBCs $\Rightarrow$ Burr cells.
- Treatment by plasmapheresis or urgent peritoneal dialysis.

Acute Post-streptococcal GN

Etiology

- It is an immune-complex disease.
- Due to infection by group A β hemolytic streptococci:
 - Pharyngeal strain 12: more in winter.
 - Skin strain 49: more in summer.

Incidence

- Age:** 5-15 years.
- Sex:** more in males.
- Course:** 2-3 weeks.

الوادر
بعض الحالات يا مشي في

Clinical Picture

History

- Of streptococcal infection 1-3 weeks ago.

The Classic Criteria of Nephritic are:

- Hematuria.
- Oliguria $< 400\text{ml} / \text{m}^2$
- Hypertension
- Edema "mild".

1. Hematuria & Oliguria:

- Dark urine + diminished urinary output is the most frequent manifestation.
- In the first few days the urine is grossly bloody then becomes smoky brown.

في الاول بيكون غامق اوى و بيمر بدم
بيبقى اخضر



2. Edema:

- Usually mild in the form of puffy eyes & edema of extremities.
- Due to:

- $\downarrow\downarrow$ GFR.
- Vasculitis $\rightarrow$ toxic capillaritis.
- $\uparrow\uparrow$ Aldosterone $\rightarrow$ salt & water retention.

- However edema may be generalized in 3 conditions.

- Associated nephritic syndrome.
- HF.
- Renal failure without restriction of fluid intake

dorsum of hands and feet.

3. Hypertension: "70% of cases"

- Due to:

- $\downarrow\downarrow$ GFR $\rightarrow$ hypervolemia.
- Vasculitis $\rightarrow$ thickening of the afferent A $\rightarrow \uparrow\uparrow$ rennin & aldosterone.

Complications

In severe cases any of the following 3 complications may occur.

1. Acute renal failure:

- Usually mild & transient in most cases.

2. Heart failure

- Due to:

- Hypertension.
- Circulatory overload.
- Toxic carditis.

3. Hypertensive encephalopathy:

- Severe headache.
- Lethargy.
- Convulsions & coma.

Investigations

1) Urine Analysis:

- Volume: ↓↓.
- ⊙ **RBCs casts (diagnostic).** لا رقيقة قشرية لحواء
- Proteinuria (mild).
- Specific gravity: ↑↑.

2) Renal functions:

- Blood urea nitrogen (BUN): ↑↑.
- Serum creatinine: ↑↑.
- Serum K⁺: ↑↑.

3) Evidence of Streptococcal Infections:

- Anti-streptolysin-O titre (ASOT): ↑↑. (in pharyngitis).
- Anti-hyaluronidase: ↑↑. (in impetigo). skin lesion - But ASOT may be Normal.
- C3: ↓↓
- Immune complexes in the blood: ↑↑.

4) Renal Biopsy:

- Light microscope: diffuse proliferative GN.
- Immuno-fluorescent microscope: lumpy deposits.
- Electron microscope: sub-endothelial deposits.

DD

A. From other causes of GN:

1. Alport syndrome (hereditary nephritis):

- AD. sensory neuron.
- GN + nerve deafness. + keratoconus
- Very young age & rapidly fatal.

causes of nephritis → 19
...! P. in the C3

2. IgA nephropathy (Berger's disease)

- Recurrent hematuria.
- Normal C3. → Cause is not immune complex.
- IgA renal deposits.
- ↑↑↑ IgA in the blood.

"Synpharyngitis" may lead to vasculitis.

3. Anaphylactoid purpura. "Henoch-Schönlein"

4. Rapidly progressive GN: renal failure within 2-3 ms.

5. Hemolytic uremic syndrome:

- Pallor due to acute hemolytic anemia.
- Uremia (Oliguria & Azotemia).
- Thrombocytopenia.

B. From other causes of hematuria:

Idiopathic hematuria or benign hematuria:

- No proteinuria.
- No Azotemia.
- No hypertension.
- Normal C3 & ASOT.

C. From other causes of edema.

D. From other causes of hypertension.

Treatment

1. Early Antibiotic Therapy:

- For streptococcal infection for 10 days.
- Dose: 400,000 U procaine penicillin. IM / 12hrs after sensitivity test.

2. Fluid Restriction:

- Volume of urine in 24 hrs + 400 ml / m² / D.

3. Diet:

- ↓↓↓ protein 0.5 gm/kg/D (may reach 2 mg).
- ↓↓↓ K → if there's RF:
- ↓↓↓ Na → if there's hypertension.
- ↑↑↑ Carbohydrate.

↓ Fat.

4. Treatment of Hypertension:

Antihypertensive drugs

- Hypertensive encephalopathy: diazoxide 5 mg/Kg/ D IV+ lasix 1 mg / kg or propranolol 1 mg / kg or hydralazine 0.1 mg/ kg IM.
- Mild or moderate hypertension: Oral diuretics as lasix ± Hydralazine or methyldopa 20 mg / kg / D.

5. Hyperkalemia

Normally K = 3.5 → 5 meq. / L.

↓ Lasix or
dialysis
Resect. dialysis line

- Glucose + Insulin 0.1 U/kg IV drip → will enter K+ intracellular.

- Ca gluconate 0.5 ml / kg I.V.

- Ion exchange resin 25 gm + 5 % glucose 100 ml rectal enema.

6. Peritoneal Dialysis:

Indications:

- Persistent Hyperkalemia.
- Severe acidosis.
- Pulmonary edema.

⊙ We give glucose & insulin for risk of hypoglycaemia.

→ K enters to ! sm ms of Bronchi → so give B2 against To
in nebulizer → avoid Broncho Constriction.

⊙ Ca gluconate :- gluconate + K → Bile.

Ca → ↓ Tachy arrhythmia "cardio protective".

Acute Renal Failure

Definition

- It is a clinical syndrome characterized by sudden reduction of glomerular & tubular functions.

1. Oliguria or anuria ($< 180 \text{ ml} / \text{m}^2 / 24 \text{ hrs}$).
2. Metabolic acidosis.
3. Impaired excretion of waste products such as creatinine, urea, K^+ and phosphate.
4. Hyperkalemia.

Etiology

1. Pre-renal (Hypovolemia)

1. Dehydration.
2. Hge. *2 and the sea*
3. Shock.
4. Post surgery.
5. Cardiac surgery
6. Nephrotic syndrome.

⇒ Hypertension

2. Renal

1. Anoxic tubular necrosis.
2. Glomerulonephritis acute or chronic:
 - Post streptococcal.
 - SLE.
 - Henoch Schonlein purpura.
 - Nephrotoxins, anesthesia, mercury and carbon tetrachloride.
 - Rapidly progressive GN.
 - Hemolytic uremic syndrome.
3. Congenital abnormalities: renal agenesis or hypo genesis.
4. Acute pyelonephritis.
5. Tubular obstruction: uric acid nephropathy & sulfonamide crystals. *renal cause 9 pr*
6. Vascular:
 - Malignant hypertension.
 - Renal vein thrombosis or DIC. *right side*
7. Severe infection.

⇒ Hypertension

renal cause 9 pr
in acute pyelonephritis
capsule

3. Post-renal

1. Congenital obstruction.
 - Posterior urethral valve.
 - Pelvi-ureteric junction obstruction.
2. Acquired obstruction:
 - Bladder neck obstruction.
 - Ureteral obstruction. *B. pt.*
 - Urethral stricture or stone.

⇒ Hypertension

Causes in the Newborn

1. Per-natal anoxia
2. RDS
3. DIC
4. Severe hemorrhage.
5. Severe dehydration.
6. Septicemia.
7. Congenital obstruction
8. Acute pyelonephritis
9. Renal vascular thrombosis
10. Hemolytic uremic syndrome.

Pediatrics**11****Clinical Picture****Tetrads**

- Oliguria or Anuria.
- Metabolic acidosis
- Azotemia
- Hyperkalemia

1. Anuria or Oliguria.
2. Acidosis.
3. Anorexia & pallor.
4. Dyspnea.
5. Uremic breathing.
6. Impaired level of consciousness up to coma.
7. Irritability up to convulsions.
8. Bleeding tendency due to platelet dysfunction.

Investigations**1. Urine:**

- Volume: < 400 ml / m² / 24 hrs.
- Specific gravity: low fixed 1010.
- Casts: RBCs & epithelial casts.
- Na:
 - < 30 mEq/L in pre-renal failure.
 - > 30 mEq/L in renal failure.
 - > 70 mEq/L in tubular dysfunction.

2. Blood Chemistry:

- Na⁺: dilutional hyponatremia.
- K⁺: Hyperkalemia "main cause of death".
- S. Urea & creatinine: elevated.
- ABG: Metabolic acidosis.
- Uric acid: ↑↑.

3. ECG:

- Hyperkalemia.
- High peaked T-wave.

4. For the Underlying Cause.**Treatment**

Measurement of blood pressure.
Initial bladder catheterization to exclude obstruction.

1. Pre-renal

- Urgent correction of Hypovolemia or shock if present by Ringer's lactate 20 ml / kg within 15 minutes ⇒ ↑↑ volume of urine, if no ↑↑ in volume of urine give mannitol 0.2 gm / kg IV within 2 minutes + lasix 1 mg / kg IV: if diuresis occurs ⇒ reversible case, if not ⇒ irreversible.

2. Post-renal

- Nephrostomy
- Then → surgery.

permanent RP. ۱۱ دایم در دسترس

mannitol or Diuretic
④ IV fluid

3. Renal

1. Restriction of fluids: urine volume in the last 24 hrs + 400ml / m² / 24hrs.
2. Treatment of Hyperkalemia: as post-streptococcal GN.
3. Treatment of hypertension if present as post streptococcal GN
4. Dialysis:
 - Severe metabolic acidosis.
 - Severe Hyperkalemia
 - Severe circulatory congestion.

Other Indications of Dialysis

- BUN > 125 mg/ dl.
- Severe hypo or hypernatremia.
- Chronic renal failure with severe symptoms.
- Poisoning by certain drugs as barbiturates, salicylates & amphetamine.
- Hemolytic uremic syndrome.

Chronic Renal Failure

Definition

- It is a clinical state in which the kidney can't maintain body homeostasis.

Etiology

⇒ In children < 5 years:

1. Renal hypoplasia. → *موجوده من غير اكتمال*
2. Renal dysplasia. → *موجوده غير طبيعية*
3. Obstructive uropathy. → *Back pressure*
4. Urinary tract malformation. →

⇒ In children > 5 years:

A. Hereditary:

1. Alport syndrome.
2. Polycystic kidney.

B. Acquired:

1. Glomerulonephritis.
2. HUS. → *Hemolytic uremic*

Clinical Picture

Uremic Manifestations

1. Headache.
2. Fatigue.
3. Anorexia & vomiting.
4. Lethargy & lack of concentration.

Urine Volume

1. Early in the disease:

- There is polyurea & polydipsia due to urinary concentration defect.

2. Late in the disease:

- Oliguria develops due to loss of a significant number of nephrons. This is usually followed by anuria due to complete loss of all nephrons.

Pediatrics**13****Air Hunger (Rapid Deep Respiration)**- It is caused by acidosis due to:

1. Loss of HCO_3 in urine.
2. Failure of excretion of acidic materials.

Complications of Uremia**1. Bone deformities & short stature (Renal osteodystrophy):**

See renal rickets (notebook of nutritional disorders).

2. Growth failure: due to:

- a. Renal osteodystrophy.
- b. Restriction of protein in diet.
- c. Chronic anemia.
- d. Uremia $\Rightarrow$ end organ resistant to GH.

3. Pallor: due to:

- a. $\downarrow\downarrow\downarrow$ Erythropoietin.
- b. Bleeding tendency.
- c. Inadequate iron & folate intake.
- d. Urea & other toxins $\Rightarrow$ hemolysis of RBCs.
- e. Aluminum intoxication $\Rightarrow$ BM suppression.

4. Cardiovascular complications:**a. Hypertension:** due to:

- Over production of rennin.
- Na^+ & water overload.
- Hyperlipidemia due to diminished activity of lipoprotein lipase activity

b. Peri-carditis: due to deposition of uremic toxins. *may lead to effusion d.t hypervol.***c. Heart failure:** due to:

- Toxic myocarditis due to uremia.
- Hypertension.
- Anemia.
- Volume over load.

*• $\heartsuit$ Tamponade d.t pericardial effusion.***5. Bleeding tendency:** due to:

- a. Thrombocytopenia.
- b. Thrombasthenia.
- c. Coagulopathies.

6. Recurrent infections: due to suppression of immune system by uremic toxins.**7. Neuropsychiatric manifestations:** due to:

- a. Uremic toxins.
- b. Hypertension.
- c. Aluminum intoxication.
- d. Trace elements & vitamins deficiencies.

*d.t dyspepsia***Manifestations Related to Underlying Etiology.****Investigations****1-Urine Analysis:**

- Polyuria.
- Low fixed specific gravity 1010

2-Urea & creatinine: elevated.**3-CBC:** normocytic normochromic anemia.*Plasma 1/3*

4-Electrolytes:

- Hyperkalemia. *end stage*
- Hyponatremia.
- Hypocalcaemia.
- Hyperphosphatemia. *uric acid ↑*
- ↑↑ Alkaline phosphatase.

5-Blood gases: metabolic acidosis.**6-Echo-cardiography:** for evaluation of the cardiac functions.**7-Assessment of bone status:**

- ↑↑↑ PTH.
- Sonar & scan for the parathyroid gland.
- Bone densitometry.

8-Assessment of nutritional status:

- Serum albumin.
- Serum transferrin.
- Serum zinc.
- Serum iron.
- Serum folic acid.
- Lipid profiles.

9-Investigation to detect the etiology.**Treatment****1. Treatment of the cause****2. Diet:**

- Caloric supply: should be made to equal or exceed (in patients with growth failure) the recommended daily caloric allowance for age. This achieved by adding to diet unrestricted amounts of CHO & fat (usually medium chain triglycerides) as tolerated by the patient.
- Proteins: if there is uremic symptoms 1.5gm/kg/day. *→ give 1 line*
- Routine supply of water soluble vitamins especially in patients under dialysis.
- No need for supplementation with fat soluble vitamins.
- Trace element supply (zinc, iron): should be added after deficiencies are confirmed.
- Calcium.
- Phosphate in diet & and use calcium carbonate as phosphate binder that enhance fecal excretion of calcium phosphate.
- Antacids containing aluminum should be avoided because of aluminum toxicity.
- Salts if there is hypertension, volume overload or congestive HF. But ↑↑ salt may be needed in salt looser types.
- K intake & oral K-chelating resin that binds to & remove potassium from the intestine. *only when urine volume ↓ ↓ "end stage"*
- Water restriction is usually needed in patients with end stage renal disease.

3. Treatment of hypertension & uremic cardiomyopathy:

See AGN.

4. Treatment of acidosis: oral NaHCO_3 is needed if serum level falls below 20 mEq/L.**5. Treatment of rickets:** See renal osteodystrophy in notebook of nutritional disorders.

6. Treatment of anemia:

Hb level should be stabilized at 10 gm% by:

- Treatment of iron deficiency.
- Treatment of folic acid deficiency.
- Treatment of zinc deficiency.
- Treatment of aluminum intoxication.
- Treatment of infections.
- Treatment of bleeding focus.
- Erythropoietin $\rightarrow$ 75U/kg.

7. Dialysis:

- Either peritoneal or hemodialysis.
- It is indicated when $GFR < 10 \text{ ml / minute}$. However, some patients need dialysis at earlier stages, as they can not tolerate the uremic state.

- Peritoneal dialysis:-

- a. Continuous ambulatory peritoneal dialysis.
- b. Continuous cyclic peritoneal dialysis using cycler machine.



8. Renal transplantation.

9. Treatment of concomitant complications.

10. Social & psychological support.

11. Drug dosage:

- All drugs excreted by the kidney their doses should be adjusted according to renal function to minimize the risk of toxicity.

Urinary Hues

Dark yellow • أصفق شوبية من الطير

1. Concentrated urine.
2. Bile pigments.

Red urine

1. Hematuria. e.g. G6PD - وأل فون
2. Hburia.
3. Urates.
4. Myoglobin. مربيع خابطه فلافو كروم
5. Porphyrins.
6. Foods as beets, blackberries, colorings.
7. Drugs: Rifampicin, chloroquine.

Dark Brown or Black

RBCs cast.

1. Homogentisic acid.
2. Melanin.
3. Methemoglobinemia.

Localization of Hematuria

	From kidney	From lower urinary tract
1. Color of urine	Brown or cola-colored.	Red
2. Relation to urine stream		May be terminal (bladder) or initial (urethra)
3. RBCs morphology	- <u>Dysmorphic</u> . - <u>RBCs casts</u> .	- <u>Eumorphic</u> - May be <u>clots</u>
4. Proteinuria	> or = 2+	< 2+
5. Associated manifestations	- Edema. - Hypertension. - Impaired renal function	- <u>Dysuria</u> . - Suprapubic pain. - Disturbed urine stream.

Hematuria

Definition

- The presence of blood in urine which may be gross or microscopic (**>5 RBCs/HPF**). *High Power Field.*

Etiology

A. Glomerular:

- Acute glomerulonephritis**: as acute post-streptococcal GN.
- Recurrent gross or persistent microscopic hematuria**:

- IgA nephropathy (Berger's disease):
 - More common in males.
 - May be high serum IgA.
 - Normal C3.
 - There is mesangial IgA deposits.

- Alport \$:

- AD or XLD.
- Age: 6 years.
- Hematuria.
- Sensory-neural deafness.
- Cataract & keratoconus.
- Progress rapidly to CRF.

- Membranous & membrano-proliferative GN.

- SLE.

- Rapidly progress GN.

- Nephritis of chronic infection: as in SBE, \$, malaria, hepatitis B. In all of these diseases there is high level of circulating immune complexes that deposit in the glomeruli.

- Hemolytic-Uremic syndrome: Caused by Vero toxin producing E-coli.

- Hemolytic anemia.
- Thrombocytopenia.
- ARF.

- Anaphylactoid purpura (Henoch Schonlein purpura).

*No minimal change
No drug.*

B. Non-glomerular:

1. Congenital anomalies:
 - Polycystic kidneys.
 - Vascular anomalies.
2. Infections: bacterial, viral, bilharzial.
3. Stones.
4. Tumor. *neoplasms or infiltration*
5. Trauma.
6. Drugs: Cyclophosphamide & anti-coagulants.
7. Exercise.

CIN DVT

Laboratory Work-up**Phase I (for All Patients)**

1. Urine analysis & culture.
2. Collection of 24 hrs urine for:
 - a. Protein.
 - b. Calcium ($n < 4\text{mg/kg/D}$).
 - c. Creatinine clearance.
3. CBC.
4. Streptococcal Abs titre.
5. Pelvi-abdominal U/S.
6. Plain X-ray on the UT & IVU.

Phase II (In Selected Patients)

1. C3 level.
2. ANA.
3. Sick cell screening.
4. Coagulation profile.
5. Ascending urethrography.
6. Audiometry.

Phase III (Invasive)

1. Renal scan.
2. Cystoscopy.
3. Renal biopsy.

Treatment

1. Supportive Treatment if hematuria is severe.
2. Treatment of the cause if possible.

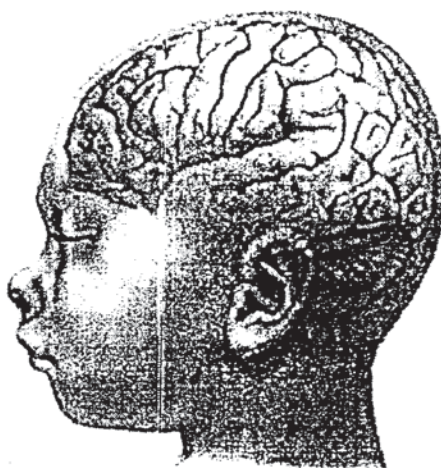
وثر بيشتر
فبیشتر

Neurology

Normal head size



Microcephaly



Hydrocephalus

In hydrocephalus the volume of CSF is increased within ventricular or sub-arachnoids spaces $\Rightarrow$ dilatation of the ventricles + $\uparrow\uparrow$ intracranial pressure in the majority of cases.

CSF- Circulation

$\Rightarrow$ next paper.

Etiology

A. Obstruction of CSF circulation (non-communicating)

I. At foramen of monoro.

- a. Congenital.
- b. Tumors.
- c. Inflammatory.

II. At aqueduct of sylvius:

1. Congenital:

- Atresia.
- Stenosis.
- Forking.
- Vein of Galen.

2. Acquired:

- Gliosis.
- Tumors.

III. At the foramen of Magendi & Lushka.

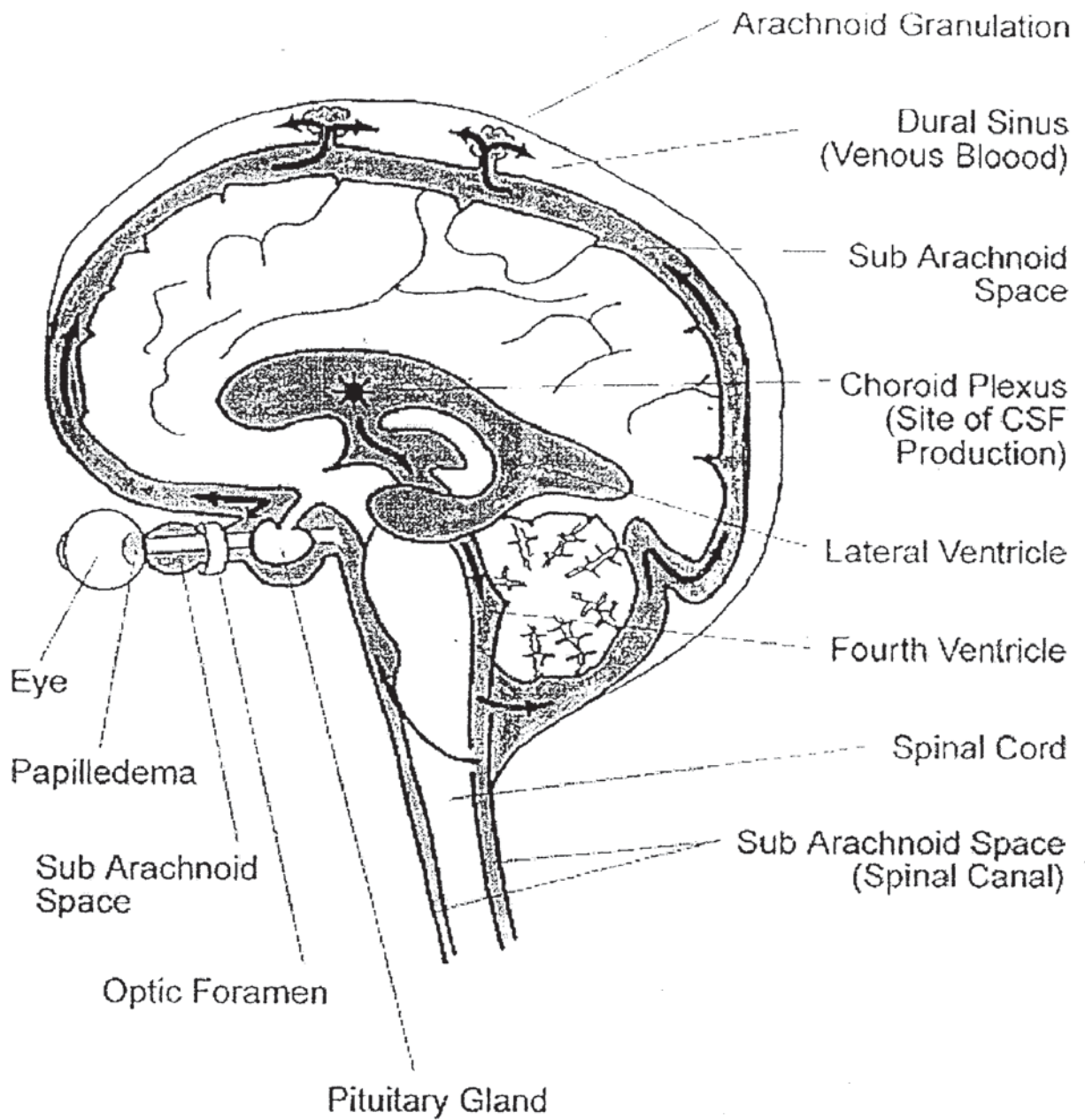
1. Congenital:- Dandy- Walker malformation.
2. Acquired:

- Meningitis.
- Hemorrhage.
- Posterior fosse tumors

B. Non obstructive (communicating):

I. Increased secretion:

1. Choroiditis.
2. Choroid congestion.
3. Pseudo tumor cerebri ..See later.
4. Meningism.



II Decreased absorption:

1. Subarachnoid hemorrhage.
2. Subarachnoid adhesions.
3. Sinus thrombosis.
4. Achondroplasia.
5. Arnold Chiari syndrome.
6. Mucopolysaccharidosis.

TYPES



A. Obstructive: There is an obstruction to the CSF Circulation between ventricles or at outlets of the 4th ventricle

B. Communicating: There is free communication between the ventricles & subarachnoid space i.e. ↑↑ production or ↓↓ absorption.

Arnold Chiari Malformation

- There is downward displacement of medulla oblongata & cerebellum ⇒ Obstruction of the subarachnoid pathways around the brain stem
- It is usually associated with spina bifida + Meningo - myelocele.

Clinical Picture

A. Before Closure of fontanels

1. ↑↑↑ Skull circumference.
2. Sutures ⇒ widely separated.
3. Fontanels ⇒ widely opened.
4. The scalp veins ⇒ dilated & visible.
5. The skin ⇒ stretched, shiny & thin.
6. Eyes ⇒ sun set appearance ⇒ why?
& Optic atrophy in long standing cases.
7. The cry ⇒ high pitched.
8. Mac Ewen's sign ⇒ resonant note upon percussion of the skull, due to separation of the sutures.
9. Craniotabes.
10. Marked occipital expansion due to dilatation of the 4th ventricles in Dandy-Walker malformation.
11. Trans-illumination of the skull may be +ve in severe cases.
12. Neurological manifestations:
 - MR ⇒ due to atrophy of the cerebral cortex.
 - Convulsions.
 - Motor retardation & UMNL.



B. After closure of fontanels

The cause is usually acquired.

1. Signs of ↑↑ intra-cranial pressure (ICP).
e.g. persistent vomiting, severe headache & papilloedema
Disturbed tone & reflexes in the form of spasticity & hyperreflexia.
2. Skull is not significantly enlarged.
3. Mentality may be less affected.

Investigations

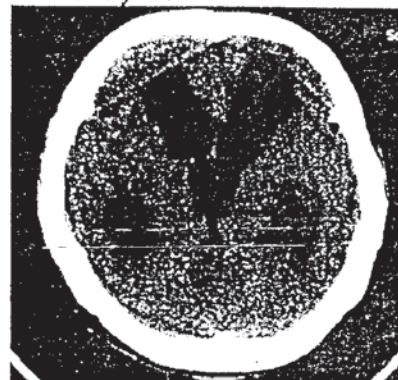
1. Plain X-ray skull

- Cranio-facial disproportion.
- Opened sutures & fontanel
- Intra-cranial calcification may be present (scattered in toxoplasmosis & peri-ventricular in CMV infection).
- Evidence of calcification in a tumor or hematoma may be present.
- Occipital bone expansion in Dandy- Walker malformation.

2. CT-Scan & MRI:

Showing $\Rightarrow$

- Size of ventricles.
- Site of obstruction.
- Pathology of obstruction.
- Extent of the disease.
- Remaining of cerebral mantle.



3. U/S of the brain: When the anterior fontanel is still opened.
4. Fundus examination: May show chorio-retinitis in congenital infection.
5. Serology: For STORCH infection.
6. Ventricular CSF pressure monitoring: Is the only accurate method to assess the activity of hydrocephalus "progressive or stationary"
7. Positron emission topography (PET):
8. Spectroscopic PET



I. From other causes of $\uparrow\uparrow$ skull circumference:

1. Rickets.
2. Achondroplasia.
3. Chronic hemolytic anemia.
4. Hydranencephaly.
5. Megalencephaly.
6. Familial.

II. From other causes of $\uparrow\uparrow$ ICP:

1. Space occupying lesion.
2. CNS infection.
3. Meningism.
4. Pseudotumor cerebri.
5. Encephalopathy.
6. Cranio Stenosis.
7. Severe hypertension.
8. Vasculitis syndromes.

Treatment

A. Observation & evaluation

1. If the patient is clinically well, with normal rate of skull growth $\Rightarrow$ continue observation.
2. In mild cases $\Rightarrow$ A trial of diuretics

B. Medical t t t (preoperative or if surgery is not indicated):

1. Diuretics e.g.
 - a. Diamox "Carbonic anhydrase inhibitor"
50 - 75 mg / kg / D $\Rightarrow$ $\downarrow$ C.S.F. Production about 1/3
 - b. Mannitol 200 mg / Kg over 20 minutes.
2. Penicillin for congenital syphilis.
3. Daraprim "Pyrimethamine" $\Rightarrow$ Toxoplasmosis.
4. Salt & water restriction.
5. Dexamethasone.
6. Anticonvulsants if there is convulsions.

C. Surgical t t t

1. Surgical removal of the cause of obstruction if possible e.g. cyst, tumors, abscess & hematoma.
 2. Shunting the CSF to by pass the obstruction:
This is done by using a one way valve Spitz-Holter valve The CSF is shunted to another site to be absorbed e.g.
 - a. Ventriculo-atrial shunt $\Rightarrow$ to the Lt atrium.
 - b. Ventriculo-peritoneal shunt $\Rightarrow$ to the peritoneal cavity.
 - c. Ventriculo—pleural shunt.
 - d. Ventriculo-cisternal shunt.
- Once a successful shunt has been established- it should be maintained for life.
3. Choroids plexectomy or diathermy coagulation $\Rightarrow$ for choroids papilloma.
 4. Third ventriculostomy in obstruction of foramen of Monroe.

Complications of shunt

A. Obstruction

Due to slipping, kinking or thrombus formation $\Rightarrow$
Manifestations of ICP

B. Infection

$\Rightarrow$ manifestations of septicemia as fever, rigors & toxemia.

C. Pulmonary embolism.

D. Focal glomerulonephritis.

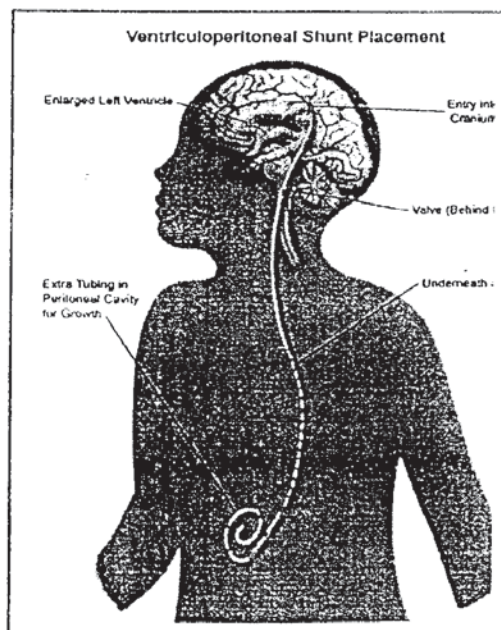
E. Chronic brain malfunctioning.

F. Shortening by age.

G. Acute shunt failure: in which there is increased ICP without evidence of obstruction or infection but symptoms improve on changing the shunt.

Causes of pseudo-tumor cerebri:

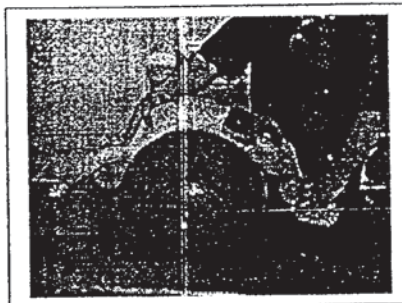
1. Hyper or hypovitaminosis A.
2. Hypoparathyroidism.
3. Hypervitaminosis D.
4. Outdated tetracycline.
5. Adolescent obese females.



Cerebral Palsy

Definition

- Non progressive central motor neuron deficit affecting the growing brain, dating to events in the prenatal, natal or postnatal period.
- Manifested since birth or early infancy.
- Prevalence 2-5 /1000 live births.
- More in LBW.



Hypertonia in C.P

Characters

1. Non fatal, non curable, non progressive.
2. Purely motor "no sensory manifestations"
3. May be associated with epilepsy, MR, deafness, speech, vision, behavioral & emotional disturbances.
4. Manifestations are present early in infancy or in the neonatal period.

Etiology

A. Ante- natal

1. Intra-uterine infections: STORCH.
2. Fetal anoxia $\Rightarrow$ Maternal hge
Placental insufficiency.
3. Maternal irradiations of the pelvis or drugs during pregnancy.
4. Congenital malformations of brain or vascular occlusion.
5. Some inborn errors of metabolism.

B. Natal

1. Birth injury $\Rightarrow$ IC hge.
2. Cerebral anoxia e.g. Hypoxic Ischemic Encephalopathy.

C. Post-natal

1. I.C. Infections: Meningitis, Encephalitis.
2. I.C. hemorrhage.
3. Neonatal asphyxia.
4. Bilirubin encephalopathy.
5. Metabolic disorders :- Hypoglycemia,
hypocalcaemia & toxins.

Clinical Picture

A. Spastic C.P.(75 %)

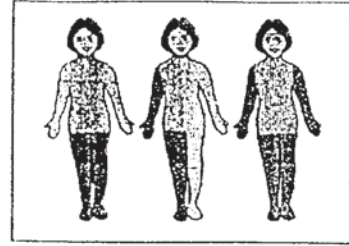
UMNL $\Rightarrow$

- Weakness or paralysis.
- Hypertonia more in the adductors $\Rightarrow$ scissoring of legs & antigravity Ms.
- Exaggerated deep tendon reflexes.
- +ve Babiniski sign
- Late muscle wasting.



• Distribution:

- Hemiplegia. *one side*
- Paraplegia. *both ll*
- Quadriplegia. *four limbs*
- Diplegia. *both upper*
- Monoplegia. *one limb*
- Double Hemiplegia. *one side of both ll*
- Biplegia. *upper of the ll*



MR ⇒ Common finding.

The most common type is spastic diplegic C.P.



B. Atonic C.P.

- Severe hypotonia.
- Normal or exaggerated deep tendon reflexes.
- MR ⇒ constant.
- High mortality.

C. Ataxic CP (1-2 %):-

⇒ Picture of cerebellar ataxia.

- Dysmetria.
- Tremors.
- Nystagmus.
- Zigzag gait.
- Dysdiadokokinesia.
- Hypotonia.



D. Extra-pyramidal CP (20 %):-

- Chorea.
- Athetosis.
- Dystonia.
- Static tremors.
- Abnormal tone ⇒ hypotonia or rigidity.

E. Mixed C.P.

Functional & prognostic classification

According to the degree of motor dysfunction:

Class I: absent.

Class II: Mild.

Class III: Moderate.

Class IV: Severe.

Investigations

A. To reach the underlying etiology:

1. Plain X-ray skull.
2. Brain CT scan & MRI may be needed.
3. Fundus examination.
4. Lumber puncture.
5. Metabolic screening as urinary plasma amino gram.
6. Serology for congenital infections.

B. For functional assessment:

1. I.Q.
2. Audiometry.
3. Psychometry
4. EEG

Treatment

1. Physiotherapy.
2. Speech therapy.
3. Special educational, social, psychological hygienic programs.
4. Nutritional rehabilitation.
5. Auditory aids.
6. Drugs which decrease the tone as baclofen, dantrolen Na, benzodiazepine, L- DOPA & alcohol
7. Anticonvulsants if there is epilepsy.
8. Surgery $\Rightarrow$ Orthopedic neurosurgery.

Abnormalities of size & shape of the skull

A. Microcranium.

B. Macrocephaly:

Macrocephaly

Definition

OFC $> 95^{\text{th}}$ centile or OFC > 2 SD for age, sex race.

Etiology

A. Cranial (thick skull bones):-

1. Chronic hemolytic anemia.
2. Rickets.
3. Osteogenesis imperfecta.
4. Osteopetrosis.
5. Hyperphosphatemia.
6. Familial.



B. Intracranial

1. Hydrocephalus.
2. Hydranencephaly replacement of the brain by CSF
3. Megalencephaly (increase in the number & size of the brain cells)
 - MPS.
 - MSUD.
 - Galactosemia.
 - Achondroplasia.
4. Porencephaly (hemispheric cyst)

Micro-cranium

Definition

It is small head with skull circum-ference less than the 3rd percentile

TYPES

A. Small brain ⇒ Micro-cephaly

B. Premature closure of the sutures ⇒ Cranio-synostosis "Cranio-Stenosis"

Microcephally

Etiology

1. Brain developmental defect:

- Primary (hereditary) AR micro-cephaly: It is characterized by backward sloping of the front.
- IEM ⇒ PKU MSUD.
- Fetal irradiation ⇒ 1st 2nd trimesters
- Fetal alcohol syndrome.
- Some chromosomal disorders as Down, Cornelia de Lange & Rubenstein Taybi syndromes.

2. Familial

3. 2ry to

- Congenital infections: STORCH-EB.
- Placental insufficiency & Peri-natal anoxia ⇒ Hypoxic ischemic encephalopathy.
- Post meningitis or post encephalitis.

Clinical Picture

1. Small skull.
2. No manifestations of ↑↑↑ ICP.
3. Early, fontanel is open.

Normal head size



Microcephaly



Investigations & Treatment

As C.P.

Cranio-Stenosis

Micro-cranium 2ry to premature closure of one or more of skull sutures.



A. Abnormal shape of the skull

This depends on the affected sutures ⇒

1. Sagittal suture: ⇒ Dolico-cephaly or scapho-cephaly.
2. Bilateral coronal suture: ⇒ Brachy-cephaly.
3. Unilateral closure of the coronal or lambdoid suture ⇒ Plagio-cephaly.
4. Closure of all sutures: Oxycephaly (pointed head).
5. Metopic suture ⇒ Trigono-cephaly triangular head with prominent vertical ridge in the mid-forehead.
6. Acrocephaly: ⇒ Tower like head with vertical forehead.

C. Manifestations of ↑↑↑ ICP.

Investigation

X-ray skull shows ⇒

- Silver beaten appearance.
- Abnormal shape of the skull.
- Bony closure of the suture.

Treatment

1. Craniotomy ⇒ opening of the suture line.
2. Craniectomy ⇒ removal of a bony strip it is very effective

Mental Retardation

Definition

It is a state of impairment of intelligence (complex mental process including thinking, memory, reasoning, verbal expression and adaptive behavior) dating from early life.

Etiology

A. Environmental

- No organic causes can be found.
- It due to socio-cultural & emotional disturbances.
- It is the most common cause of MR in about 90% of cases.
- It is usually mild.

B. Organic causes

1. Pre-natal natal
2. Chromosomal abnormalities
e.g. Trisomy 21, 18, 13 & deletion 5P - , 4P-.
Fragile X- Chromosome
3. Post-natal ⇒ as CP.+
 - Cerebral laceration due to head trauma.
 - Infections as meningitis or encephalitis.
 - Cerebro-vascular accident,
 - Post-immunization encephalopathy e.g. Pertussis.
 - Poisoning e.g. Carbon monoxide.
 - Metabolic as severe hypoglycemia.

Degrees of MR

Degree	Term	IQ	Prognosis	Incidence
Mild	Moron	50-70	Educable	85%
Moderate	Imbecile	35-50	Trainable	5-10%
Severe	Idiot	20-35	Non-trainable 5%	
Profound	Idiot	0-20		

In some literatures moderate is referred to as high imbecile & severe as low imbecile.

How to calculate the IQ:

1. Assess the mental age by the developmental history. If level of different parameters are near to each others, consider the average.
 2. If there is marked discrepancy the socio-adaptive history is the most important.
- $$IQ = \frac{\text{Mental age}}{\text{Chronological age}} \times 100$$

Manifestations of MR:

1. Delayed development of milestones & sphincter control.
2. Impaired learning ability.
3. Poor social adjustment.

Investigations & Treatment

As CP except no need for physiotherapy.

Hypotonia & neuromuscular diseases

Tone is the resistance of the muscle to stretch and the muscle is said to be hypotonic or flaccid when it offers little resistance to stretch.

Diseases affecting the anterior horn cells

- A. Poliomyelitis: see notebook of infection.
- B. Spinal muscular atrophy.
- C. Amyotrophic lateral sclerosis: -very rare.
- D. Pena-Shokeir & Marden-Walker syndromes there is degeneration of motor neurons + arthrogryposis + multiple congenital anomalies.

Spinal muscular atrophy

Etiology

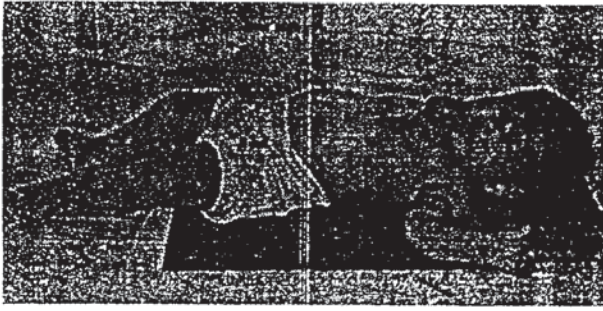
AR disease $\Rightarrow$ intrauterine degeneration of motor neurons.

Types

1. Infantile SMA (severe) $\Rightarrow$ Werdnig Hoffman.
2. Late infantile SMA 2 (mild).
3. Juvenile SMA3 (chronic).
4. Fazio-Londe $\Rightarrow$ bulbar more than spinal.

C/P of Werdnig Hoffman disease

1. Both sexes are affected.
2. +ve Family history + history of consanguinity.
3. History of weak fetal kicks.
4. After birth there is:
 - Weakness or paralysis.
 - Hypotonia.
 - Hypo-reflexia.
 - Later muscle wasting.
 - Distribution: All these findings are bilateral, symmetrical, proximal as distal.
 - Marked muscle fasciculations especially in the tongue.
 - Bulbar affection $\Rightarrow$ nasal tone of voice, nasal regurgitation of food, hoarseness of voice, dysphagia & repeated choking.
 - Staring look due to sparing of extra ocular & facial muscles.
 - Normal sphincters & intelligence.



Werding Hoffman disease

Investigations

1. EMG $\Rightarrow$ Neuropathic.
2. Nerve conduction velocity (NCV) $\Rightarrow$ normal.
3. Serum CPK: normal.
4. Muscle biopsy: picture of early denervation.

Treatment

Supportive ttt because there is no available ttt up till now. Some of later presenters may be trained to use computer.

Guillain Barre Syndrome (Post- infections polyneuropathy)

Etiology

- Auto-immune post-infectious disease affecting the myelin sheath.
- It usually follows measles, chicken pox or influenza.

Clinical Picture

1. History of viral infection 1-3 weeks before the onset of the disease.
2. Acute motor weakness starting in the L.L. $\Rightarrow$ trunk $\Rightarrow$ UL $\Rightarrow$ bulbar "Landry's ascending paralysis"
3. Distribution: Usually bilateral, symmetrical, distal more than proximal of LMNL.
4. Tender calf ms.
5. Gloves & stoking hypothesia.
6. Others.
 - a. Bulbar palsy & other cranial Ns.
 - b. Respiratory affection.
 - c. Autonomic $\rightarrow$ Labile BP & HR
 - d. Encephalitis "Encephalo- myelo-radiculopathy cranialis" + papilloedema.
7. Chronic course may occur.

Investigations

1. EMG $\Rightarrow$ Neuropathic pattern.
2. Nerve conduction velocity $\Rightarrow$ Impaired.
3. CSF examination: cyto-albuminous dissociation
Oligo-clonal gammopathy.
4. Nerve biopsy: in chronic cases.

Treatment

Self limited in most cases

1. Steroid therapy.
2. IV immunoglobulin or prednisone pulse therapy.
3. Plasmapheresis.
4. Support of vital systems.
5. physiotherapy.

Other causes of polyneuropathy

1. Traumatic: Erb's palsy (neonatology), phrenic nerve palsy.
2. Peroneal muscular atrophy.
3. Refsum's disease.
4. Leukodystrophies.
5. Neurofibromatosis.
6. Toxic neuropathies: lead poisoning, arsenic, chemotherapeutics, INH.
7. Leprosy.
8. Vitamin B1, B6 & B12 deficiency.
9. Endocrinal as DM.
10. Familial dysautonomia.
11. Congenital insensitivity to pain.
12. Interstitial hypertrophic polyneuropathy.

Myasthenia Gravis

Types

1. **Congenital MG:** Due to congenital absence of acetyl choline receptors.
2. **Juvenile MG:** Autoimmune.
3. **Neonatal MG:** Infant of juvenile myasthenia mother.

Juvenile Myasthenia Gravis

Definition

A disease characterized by easy fatigability on repetition of muscular activity which is relieved by prostigmine.

Etiology

An auto-immune disease, where there are Antibodies directed against the motor end plate & compete with the action of Ac.ch.

C/P

The disease affects the skeletal ms in a descending manner.

A. Ocular type

Ptosis, diplopia & squint by the end of the day.

B. Bulbar type

- Dropping of the jaw after prolonged chewing.
- Dysphagia & regurgitation of food from the nose.
- Dysarthria & nasal tone after prolonged talking.

C. Generalized type

- UL more involved than LL
- Proximal ms more than distal one.
- Respiratory muscles may be involved $\Rightarrow$ Dyspnea.

D. May be associated with:

- Thyrotoxicosis or hypothyroidism due to Hashimoto's thyroiditis.
- Thymic hyperplasia or adenoma.

E. Myasthenic crises:

Usually precipitated by infection, operation or idiopathic $\Rightarrow$ Severe respiratory distress

Diagnostic tests

1. **Induction of fatigue** $\Rightarrow$ by repetition of movement.
2. **Walker's test**
 - Apply sphygmomanometer cuff to one arm & raise above the systolic BP $\Rightarrow$ let the patient moves his fingers till fatigue.
 - When cuff is removed $\Rightarrow$ Ptosis occurs within 10 sec.
3. **Prostigmine "Neostigmine" test**
IM Prostigmine $\Rightarrow$ improvement after 15 mm.
4. **Edrophonium test**
IV Edrophonium $\Rightarrow$ improvement after 2 mm.

Investigations

1. EMG $\Rightarrow$ Reduction of amplitude on repetition of movement.
2. CXR $\Rightarrow$ May show Thymic shadow enlargement.
3. Thyroid profile
4. Anti Acetyl choline Antibodies.

Treatment

A. Cholinesterase inhibitor drugs.

- Neostigmine.
 - 0.04mg / kg I.V
 - 0.4 mg / kg oral
- Pyridostigmine.
 - Toxicity $\Rightarrow$ cholinergic crises.

B. Steroid therapy

C. Plasma pharesis

Other causes of neuromuscular junction blockade

A. Botulism.

B. Organo-phosphorus compound poisoning.

D. Tic paralysis

- History of exposure to tic bite.
- Usually quadriplegia with shock stage.

Myopathies

Definition

These are diseases characterized by degeneration of muscle fibers & replacement by fibro-fatty tissues.

Etiology

I. Congenital:

1. Myo-tubular myopathy.
2. Nemaline myopathy.
3. Central core myopathy.
4. Mitochondrial myopathy.
5. Amyoplasia
6. Benign congenital hypotonia
7. Arthrogryposis multiplex congenita
8. Torticollis

II. Endocrinal & metabolic disorders:

1. Hypothyroidism (Kocher Debre Semi-laigne Syndrome).
2. Hyperthyroidism.
3. Hyperparathyroidism.
4. Steroid induced myopathy: Cushing syndrome.
5. Potassium related periodic paralysis.
6. Glycogen storage disease.
7. Vitamin E deficiency.

III. Inflammatory:

1. Dermatomyositis.
2. Polymyositis.
3. Viral myositis.
4. Parasitic myositis.

IV. Muscular dystrophy: characterized by 4 criteria.

- ♦ 1ry myopathy.
- ♦ Genetic basis.
- ♦ Progressive.
- ♦ Muscle fiber degeneration & degeneration.

1. Duchenne.
2. Becker's
3. Facio-scapulo-humeral.
4. Limb girdle myopathy.
5. Ocular myopathy.
6. Myotonia dystrophica.

Pseudo-hypertrophic Type (Duchenne myopathy)

Genetics

XLR "X P 21"

The gene is related to the Dystrophin protein of the sarcolemmal membrane. It is present in the muscles (skeletal & smooth), heart & brain, all of which are affected in the disease.

Patho-Physiology

- In myopathy the muscles are unable to convert creatine to creatinine to get energy.
- So $\Rightarrow$ there will be deficiency of energy $\Rightarrow$ degeneration of muscle fibers which are replaced by fibro-fatty tissue.
- According to the amount of fibro-fatty tissue we may get atrophy or pseudo-hypertrophy
- The creatine which is not converted excreted as such in urine.

C/P

Age of onset 5-15 years

A. Muscle weakness or paralysis of LMNL

- Bilateral, symmetrical affection of proximal ms.
- Hypotonia & hypo-reflexia.
- Winging of the scapulae $\Rightarrow$ "due to weakness of serratus anterior"
- Exaggerated lumbar lordosis & +ve Gower sign $\Rightarrow$ "due to weakness of extensors of the trunk"
- Pot belly abdomen $\Rightarrow$ "due to weakness of abdominal muscles"
- Waddling gait $\Rightarrow$ due to weakness of gluteus medius & minimus".
- +ve Slipping sign.
- Cardiomyopathy is nearly constant.
- Intellectual impairment is constant, but MR is present in only 20-30%
- Epilepsy more than in normal population.



lumbar lordosis, Pot belly abdomen

The following muscles never to be affected:

1. Sternomastoid muscles.
2. Upper fibers of trapezius muscle.
3. Clavicular head of pectoralis major

B. Pseudo — hypertrophy of some muscles.

- 1.L.L. $\Rightarrow$ calf & gluteus medius.
- 2.U.L. $\Rightarrow$ Triceps, Deltoid, Supra & infra-spinatus.

C. No sensory or sphincters affection.

D. Skeletal deformities.

- Pes cavus
- Kyphoscoliosis.

Causes of death

1. Pneumonias.
2. Intractable HF.
3. Sleep apnea.
4. Frequent aspiration.
5. UTI.

Investigations

1. EMG $\Rightarrow$ myopathic pattern .
2. Muscle biopsy $\Rightarrow$ replacement of the muscles by fibro-fatty tissues.
3. Enzymes $\Rightarrow$ $\uparrow\uparrow$ CPK, $\uparrow\uparrow$ Aldolase, $\uparrow\uparrow$ SGOT
4. Urine analysis $\Rightarrow$ $\uparrow\uparrow$ creatine & $\downarrow$ creatinine.
5. Pre-natal diagnosis $\Rightarrow$ by detection of the specific gene "XP21"
6. ECG & Echo-cardiography $\Rightarrow$ for cardiac affection.
7. Mothers of cases usually carriers & can be diagnosed by detection of slight increase of CPK or by genetic study.

Treatment

No hopeful t t t

1. Physio- therapy
2. Care of nutrition.
3. Recently $\Rightarrow$ Gene therapy & myoblast transplantation.
4. t t t of complications $\Rightarrow$ Pneumonia – HF - UTI.

Becker's Myopathy

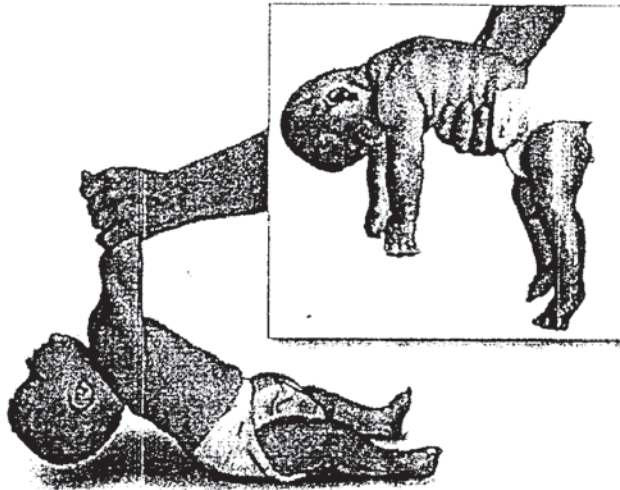
Very similar to Duchenne

Except:

1. More gradual course & delayed age of presentation.
2. Death is delayed to the late twenties.

Floppy baby

Floppy infant is an infant with severe persistent hypotonia present at birth or in early infancy.



Q1: How to diagnose floppy infant?

Diagnosis of severe hypotonia depends on the presence of the following signs:

1. **Frog-leg position** : In supine position , the limbs are abducted and slightly flexed simulating frog legs. This denotes hypotonia of limbs.
2. **Curved trunk on ventral suspension** : When the baby is suspended in prone position over the examiner's hand , he droops around it. This denotes hypotonia of the trunk muscles.
3. **Head lag**: When the baby is pulled up from his hands , while in supine position , the head lags backwards. This denotes hypotonia of neck muscles.
4. **Vertical suspension**: When hypotonic infant is suspended vertically, the head falls forwards, the legs dangle and the infant may slip through the examiner' s hands because of weakness in shoulders.

Q2 : Is it central or neuromuscular?

Clinical differentiation between central and neuromuscular causes depends on deep tendon reflexes and mental development.

1. **Central causes:** characterized by:

- Normal or exaggerated reflexes.
- MR is common.
- Abnormal brain function e.g. marked decrease in level of consciousness & recurrent convulsions may be present.
- Dysmorphic features in chromosomal disorders.

2. **Neuromuscular causes:** are characterized by:

- Weak or absent tendon reflexes.
- Normal mentality.
- Muscle atrophy suggests motor neuron disease.
- Combination of atrophy & fasciculation is a strong event of denervation.
- No other organ malformation except joint & bone structures.

Causes of floppy baby

Central

1- CP

Atonic
Ataxic

2-Chromosomal

Cri-du-chait
Trisomy 13
Down

3- Others

Lowe\$
Pradder Willi

Peripheral

Spinal cord

Werdnig Hoffmann
Extensive polio
Meningo-myelocoele.

P.N.

G.B. \$
Post-diphtheritic
Lead poisoning.
Drug induced.
Axonal neuropathy.

MNJ

-M.G.
- Organophosphates toxicity.
- Botulism.
- Tick paralysis

MS

Myopathy:
Congenital.
Metabolic.
Inflammatory
Dystrophy

Causes of inability to walk

I. Non paralytic causes:-

1. Physiological delay.
2. Mental retardation e.g. Down syndrome, cretinism.
3. Bone diseases e.g. rickets.
4. Painful limb condition e.g. arthritis, osteomyelitis, Scurvy due to subperiosteal Hge.
5. Bad general condition e.g. malnutrition, chronic illness.
6. Congenital hip dislocation

II. Paralytic causes:-

1. Cerebral causes:-

- ♦ Cerebral palsy.
- ♦ Hydrocephalus.
- ♦ Post-meningitis or post-encephalitic sequellae.
- ♦ Post-traumatic sequellae.
- ♦ Post-hemorrhagic sequellae.

2. Spinal cord causes:-

- ♦ Poliomyelitis.
- ♦ WHD.
- ♦ Meningo myelocoele.
- ♦ Transverse myelitis.
- ♦ Pott's disease.
- ♦ Spinal cord trauma.

3. Peripheral neuritis:- as floppy baby.

4. Myopathies:-

- ♦ Congenital Myopathies.
- ♦ Inflammatory Myopathies.
- ♦ Muscular dystrophies.

Intracranial hypertension

It is the rise of ICP > 15 mmHg.

Causes:

1. Cranio synostosis.
2. Intracranial space occupying lesion.
3. Intracranial infection.
4. Meningism.
5. Vasculitis & hypertensive encephalopathy.
6. Pseudo-tumor cerebri..... see before.

It is syndrome of:-

- ♦ High ICP.
- ♦ Normal CSF content.
- ♦ Normal brain.
- ♦ Normal or small ventricles.

It is called benign as spontaneous recovery generally occurs, however serious visual complications may occur.

Diagnosed after exclusion of other causes of increased ICP.

Neurological complications of failure of extra-uterine adaptation

1. Hypoxic ischemic encephalopathy (HIE).

2. I.C He due to:

- ♦ Birth injuries.
- ♦ HIE.
- ♦ 1ry hemorrhagic disturbances.
- ♦ Congenital vascular anomalies.
- ♦ Fragile vessels as in premature.

3. CNS infections as meningitis due to :-

- ♦ Defective immunity.
- ♦ Different technical maneuvers in the neonatal ICU.

4. Bilirubin encephalopathy due to

- ♦ Excess unconjugated Bilirubin load.
- ♦ Defective blood brain barrier.
- ♦ Precipitating factors as hypoxia, acidosis, hypothermia or hypoglycemia.

5. Endocrinal abnormalities as congenital hypothyroidism.

SEIZURES

Terminology

- Seizure :paroxysmal cerebral dysrrhythmia.
- Convulsions : motor seizure.
- Fit: one attack.
- Epilepsy: recurrent seizures unrelated constantly to fever or brain insult.
- Tonic convulsions: continuous muscle contractions.
- Clonic: repetitive contraction and relaxation.
- Myo- Clonic: jerky like movements which are stereotypic but not eventually rhythmic.

Etiology of seizures:

1. Congenital brain abnormalities as Microcephaly, lessencephaly.
2. Infections
 - Meningitis.
 - Encephalitis.
 - Both.
 - Abscess.
 - Sinus thrombosis.
3. Vascular
 - Embolism.
 - Thrombosis.
 - Vasculitis.
4. Tumors 1st or 2nd.
5. Head trauma concussion or lacerations.
6. Encephalopathy's, e.g.
 - * Hepatic.
 - * Water intoxication.
 - * Renal.
 - * Lead.
 - * Hypertension.
 - * CO₂.
 - * Hypoxic.
 - * CO
7. Metabolic, e.g.
 - Hyponatremia.
 - ↓ Ca
 - ↓ Mg
 - ↓ glucose
 - B6 deficiency.
 - B6 dependency.
 - Inborn errors of metabolism.
8. Other space occupying lesions as: Cyst or tuberculoma.
9. Neuro-degenerative diseases.
10. Idiopathic.
11. Febrile convulsions.
12. Drugs as digoxin, amphetamine, and analeptics.

Clinical classification of epilepsy:

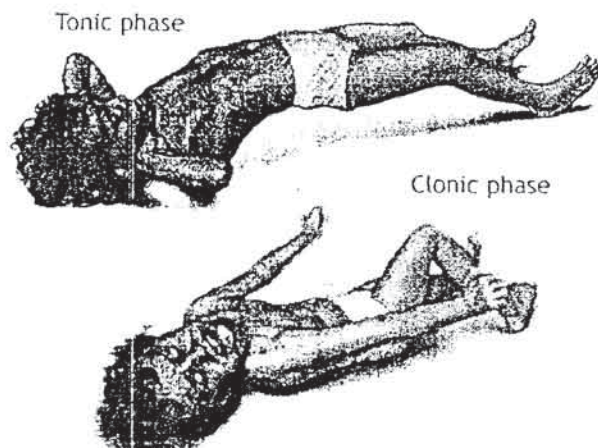
I. Generalized:

- Absence.
- Tonic.
- Myo -Clonic.
- Infantile spasms.
- Tonic Clonic.
- Clonic.
- Atonic

II. Partial.

- Simple
 - * Motor.
 - * Sensory
 - * Autonomic.
 - * Psychic.
- With secondary generalization.
- Complex.

III. Unclassified



(1) Simple partial:

(No loss of consciousness)

- Motor $\Rightarrow$
- Sensory $\Rightarrow$ Jacksonian fits.
- Psychic
- Autonomic $\Rightarrow$ abdominal epilepsy

(2) Complex partial (loss of consciousness):

aura $\Rightarrow$ automatism.

(3) Absence seizures:

A. Simple = Petit mal.

B. Complex = motor activities.

It might be associated rarely with falling.

(4) Generalized tonic Clonic seizures.

- $\Rightarrow \pm$ aura.
- $\Rightarrow$ epileptic cry
- $\Rightarrow$ tonic $\Rightarrow$ seconds
- $\Rightarrow$ Clonic.

Febrile convulsions

It is fever-related convulsions which cause is not yet settled.

Criteria

- Age: 3m- 5 years.
- Neurologically free before and after
- EEG normal 2 weeks after.
- Very high fever $> 38.8^{\circ}\text{C}$.
- Rapid rise of temp.
- Infection should not be central (extra-cranial).
- Attack lasts: seconds $\Rightarrow$ 10 mm (not $> 15\text{mm}$).
- No recurrence in, one fever (allowed once within 12 h).
- Recurrent seizure attacks can be up to 3 times (some say 5).
- Seizures are Clonic & generalized.

It may turn to epilepsy if the following risk factors were present:

1. +ve family history.
2. Onset < 9 m. age.
3. Prolonged or atypical.
4. Delayed development.
5. Abnormal neurological signs.

Treatment

- Control of fever
- Treatment of cause.
- Short term anticonvulsants.
- Avoid fever later.

DIAGNOSIS OF CONVULSIONS

Age Consideration

1. Neonatal
 - Trauma
 - Intra-cranial hemorrhage
 - Hypoxia
 - Metabolic
 - Congenital anomalies
2. 6 m—5 years —
 - Febrile convulsions
 - Breath holding attacks
 - Then other causes.
3. After 5 years
 - Idiopathic epilepsy
 - No febrile convulsions
 - Others.

Course of Convulsions

1. Acute non recurrent

- Febrile
- Trauma
- Infections
- Toxic
- Cerebral edema
- Metabolic
- Other encephalopathy's

2. Chronic recurrent

- Idiopathic epilepsy
- Tumors
- Neurodegenerative.
- Epilepsy like states---
- Hysteria
- Narcolepsy
- Cataplexy
- Migraine

Associated Features:

1. Signs of meningitis.
2. Type of seizures.
3. Neurological abnormalities
4. Mental retardation.

Investigations of seizures:

1. 1.EEG False +ve
± Prolonged EEG monitoring with simultaneous closed circuit video recording.
± Brain mapping.
2. CT or MRI if focal
3. Angiography or Doppler.
4. CSF study.
5. Biochemical studies.
6. Fundus examination.

Treatment

Is it seizure?

- (I) No = paroxysmal non epileptic
 1. Benign paroxysmal vertigo.
 2. Breath holding.
 3. Cough syncope.
 4. Familial choreo-athetosis
 5. Narcolepsy.
 6. Night tremors.
 7. Rage attacks.

(II) Yes $\Rightarrow$

i. First attack $\Rightarrow$ EEG, CT and CSF (usually febrile and metabolic)

1. Abnormal $\Rightarrow$ treatment of the cause

- Anti epileptic drugs in acute phase.
- Observation.

2. All normal $\Rightarrow$ Observation.

3. Normal except EEG $\Rightarrow$ Classify seizure type.

ii. Recurrent search for a cause and classify seizure type into either good responders or poor ones.

1. Maintain cardiopulmonary function.

2. Anticonvulsant drugs in acute stage status epilepticus.

a) Diazepam or Lorazepam IV or rectal. then

b) Phenytoin 15 - 20 mg/kg IV short very slowly 1 mg/kg/mm, then
5- 8 mg/kg/day divided on two doses.

Some centers use phenobarbitone before phenytoin if diazepam was ineffective.

c) Diazepam drip or Paraldehyde or General anesthesia.

3. After control $\Rightarrow$ follow up drugs, see table

4. ACTH usually in infantile spasm.

5. Ketogenic diet.

6. Surgery.

b) If viral was suspected.

* Virus isolation e.g.

- CSF $\Rightarrow$ Herpes simplex hominis, rubella, entero-virus.

* Serology $\Rightarrow$ 1gM (= recent fetal source).

$\Rightarrow$ IgG (maternal source).

3. Routine:

a) CBC:

* $\uparrow$ or $\downarrow$ TLC or Normal

* Band cells.

* $\downarrow$ Platelets

* Shift to left.

* $\uparrow$ ESR

b) $\uparrow$ C-reactive protein.

c) Liver, renal functions.

4. Imaging:

a) X-ray chest (even without pulmonary symptoms).

b) X-ray long bones.

c) X-ray skull calcified (Cytomegalovirus & toxoplasma)

d) Ultra-sonography for the abdomen and skull.

Treatment

I. Antibiotics:

* Immediate.

* Aggressive (doses calculated according to age;).

* According to culture & sensitivity or broad spectrum combination.

* Bactericidal.

* Take your samples before treatment.

* Best combinations are:

▪ Penicillin + amino glycosides.

▪ Penicillin + 3rd generation cephalosporins.

* Better IV. or even drip.

* Continue the course 2 weeks or at least 5-7 days after response

* If no response in 2 days:

- Change the drugs or think of pus collection.

II. Supportive treatment:

* Fluid and electrolytes (take care of SIADH).

* Blood product therapy.

* Treatment of D.I.C.

* Exchange transfusions or granulocyte transfusion.

* Assisted ventilation.

* IV immunoglobulins.

* Fibronectin therapy.

Antibiotics according to their capability to pass blood brain barrier and their safety in the newborn:

1. 3rd generation cephalosporins

2. Penicillin.

* Non inflamed meninges (do not pass).

* inflamed meninges (pass).

NEONATAL MENINGITIS

Definition

Infection of the lepto-meninges of the newborn infants.

Etiology

1. common: (Early < 1 week).

E.coli & group B streptococcus are most common.

2. Less common (late > 1 week):

* Staph. Aureus

* Klebsiella

* Pseudomonas

* Proteus

* Listeria monocytogenes

Route:

1. Early onset:

⇒ Amniotic fluid ⇒ severe form

⇒ birth canal ⇒ severe form

2. Late onset: ⇒ from community.

Clinical Picture:

- Usually non-specific, so that the need for scoring system was essential (sepsis score). Local features are rare if ever.

- General:

- Not doing well.
- Weak suckling
- Vomiting
- Sclerema neonatorum.
- Poor control of temperature
- Lethargy.
- Sluggish neonatal reflexes.

- Local:

- Irritability
- Hypertonia
- Hypo or hyperreflexia
- Abnormal neonatal reflexes.
- Hypotonia
- Tremors or seizures.
- Bulging fontanel.

Complications:

- * DIC * Shock * Heart failure * NEC * Cardiac arrest
- * Syndrome of inappropriate anti-diuretic hormone secretion.
- * Cerebral palsy, MR or epilepsy later if survived.

Diagnosis

1. Maternal history: e.g. - Prenatal rupture of membrane.

2. Identification of the causative organisms:

* Culture ⇒ bacteria

* Serology ⇒ virus.

a) If bacteria was suspected ⇒

* Gram stained smear of different specimens; blood, CSF, etc.

* Blood, CSF ⇒ culture and sensitivity.

* Counter immune-electrophoresis ⇒ rapid detection of bacterial agents.